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JULY, 1929

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THE AMERICAN PEDIATRIC SOCIETY AND PREVENTIVE PEDIATRICS *

HENRY L. K. SHAW, M.D.

ALBANY, N. Y.

The first scientific session of the American Pediatric Society was held at the Arlington Hotel in Washington in 1888. The object of the organization, as stated in the constitution, was "the advancement of the knowledge of physiology, pathology and therapeutics of infancy and childhood," and this has not been changed in the forty-one years that the society has existed.

Abraham Jacobi of revered memory was the first president, and in his address he outlined a broader vision of the field of pediatrics than was then held. He pointed out the need for medical inspection and health supervision of the schools long before they became an accomplished fact, and at that time urged the participation of members of this society in "activities which would promote the health, welfare and happiness of the people." In his presidential address in 1914, Hamill used as his text a quotation from what he happily termed "Jacobi's first epistle to the pediatrists" which will bear repetition at this time. "Questions of public hygiene and medicine," he said, "are both professional and social. Thus every physician is by destiny a political being in the sense in which the ancients defined the term, viz., a citizen of the commonwealth with many rights and responsibilities."

General topics relating to child hygiene and the history, literature and teaching of pediatrics have been the subject of 25 of 40 presidential addresses, while of 1196 papers presented in the scientific program during the past forty years only 68, in their widest interpretation, have been concerned with child hygiene.

Following a distinguished precedent, I will confine my remarks to our mutual and personal relation with what is now generally termed preventive pediatrics. A hunt through the files of our transactions reveals the fact that the society as an organization took definite action in several phases of this subject and recognized its responsibility in this wider field.

A "Committee on Welfare of Children," consisting of Drs. Jennings, Jacobi and Abt, was appointed in 1905. This was a result of the presi-

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dential address of Dr. Jennings, who urged active participation in school hygiene and national sanitation. He said, "until the American Pediatric Society gives its aid to such problems it will have but partially fulfilled its duty to scientific medicine and the welfare of the children of the Nation." The objects of the committee were to look after the general and hygenic interests of children and especially to represent the society in conferences with committees of educational and legislative bodies. A careful search through the transactions following the meeting failed to show any report of meetings or of the work of this committee.

Dr. Edsall, in his presidential address in 1910, seems to have aroused interest in child hygiene. He urged the members of the society to "engage in matters that favorably affect the welfare not only of those individuals with whom they come in immediate contact, but rather the public at large." As a result a committee on child hygiene composed of Drs. Jennings, Rotch and Hamill, and a committee on infant mortality consisting of Drs. Holt, Churchill and Knox were appointed, but no reports from either of these committees can be found in the transactions. Both apparently failed to illuminate pediatric ignorance on these subjects. At the same meeting, the society officially indorsed the activities of the Russell Sage Foundation in matters of child hygiene.

Dr. Carr, in his presidentail address in 1912, made a plea "to have representatives chosen by the society to affiliate with child welfare organizations, advise in problems of social, economic and pedagogic import and give information on the physical needs of the growing child and the dangers of pathogenic influences." Again a committee was authorized which was to have been appointed by the president to confer with the Russell Sage Foundation with regard to its work on infant hygiene and infant mortality. The minutes of the meeting do not show that this committee was appointed, and correspondence with persons connected with the foundation at that time fails to reveal information regarding any action on the part of this committee or of the foundation.

When Dr. Hamill was president in 1914, he made a noteworthy address in which he reviewed the attitude of the society toward child hygiene since its organization. This address resulted in stimulating the members to adopt a program of definite action in place of indefinite indorsement. Three committees were appointed: one on child labor composed of Drs. Van Ingen, Shaw and Wilcox, the second on cooperation with the Children's Bureau to which Drs. Hamill, Holt and Chapin were named, and a third to study the problem of vulvovaginitis, consisting of Drs. Fife, Carpenter and Gittings. The committee on child labor made a preliminary report which was published in full in the transactions. The committee was continued, but no final report was presented because the three members of the committee were called into active service in the army when the United States entered the World War. The committee on vulvovaginitis made two exhaustive and valu-

able reports which were the result of careful and painstaking work on the part of the chairman and his associates and which today stand as an authoritative contribution on this subject.

THE SOCIETY AND THE WORLD WAR

With the entrance of our country into the World War in 1917, this society work took steps to render definite service. A committe composed of Drs. Talbot, Hamill, Sedgwick, and Lucas was appointed by President Churchill "to cooperate with the Council of National Defense and to formulate plans and to indicate to the Government ways in which the American Pediatric Society could best serve the country." This committee made an exhaustive report with definite recommendations which were unanimously adopted by the society.

The 1918 meeting might well be termed the War Meeting of the society. An appeal for members to join the Medical Reserve Corps was made by Colonel Frothingham and Major Price. Six members (Drs. Fife, Gittings, Shaw, Van Ingen, Veeder and Wilcox) had already enrolled in this service, and while many others would have volunteered they sacrificed their personal desires at the request of the Council of National Defense. The council urged that teachers of pediatrics in the medical schools and pediatricians engaged in hospital work should not enter military service but should devote their energies to solving the problems of infant and child hygiene and to safeguarding the child life of the nation.

At this meeting, the society adopted a resolution "expressing its admiration for the great work the Red Cross is accomplishing" and "affirming its unswerving loyalty to it." A committee consisting of Drs. Holt, Talbot and Lucas was appointed to urge the appropriation of $100,000 to assist in the development of child welfare work and to consolidate existing agencies then engaged in this work in the United States.

Dr. Lucas urged the society to take an active part in stimulating child welfare work both in this country and abroad. He spoke of the work of the Children's Bureau of the Red Cross in France of which he was the head, assisted by Drs. Knox and Haynes. Other members of the society serving with the Red Cross included Drs. Cooley, Grulee, Ladd, Park, Ramsey and Sedgewick.

The standing committee on child welfare appointed in 1910 was discontinued, and a new committee was named to take its place. It was called the War Emergency Child Welfare Committee of the American Pediatric Society and on it Drs. Talbot, Holt, Hamill, Sedgewick and Howland served.

Our society can well feel proud of its war record and its activities in the preservation and protection of child life and health in this coun-

try and Europe. When weighed in the balance of national need, it was not found wanting. Collectively and individually, it gave substantial support and unselfish service in helping to solve the complex problems of child life which inevitably arose as a result of the great international crisis.

A resolution was passed at the 1918 meeting "to express to the Association for the Study and Prevention of Infant Mortality the hearty appreciation of the work of the Association and, moreover, to extend to the Association in every way possible the support and cooperation of the American Pediatric Society."

CHILD HYGIENE

In 1919, Dr. Richard Smith was elected the official representative of this society on the Medical Advisory Board of the Children's Bureau, a position to which he has been annually reelected and in which he has done helpful and valuable service. At this meeting a committee was appointed with the definite object of preparing a syllabus and outlining a course on child hygiene for introduction into the medical schools. The committee consisted of Drs. Richard Smith, Hamill, Helmholz, Marriott and Van Ingen. In a paper on child welfare work, read by Talbot at this meeting, he stated that "a world-wide child welfare campaign was one of the most urgent needs of the day" and that he considered "child welfare an essential part of preventive medicine which cannot be separated from it."

The report of the committee on the preparation of a child hygiene syllabus was presented to the society in 1920. This gave in detail an outline for didactic instruction in preventive pediatrics and child hygiene. The committee made the following recommendations: "The last few years have emphasized as never before the necessity for preventive work with children and the recent draft made clear that the practice heretofore in vogue with reference to the case of normal individuals did not produce satisfactory results. If we are to secure a really healthy generation the work must begin with the children. Physicians must be the ones to give advice. It is extremely desirable for the medical schools to give more definite instruction with reference to the care of normal children and this outline is suggested to this end."

The importance of this report cannot be overemphasized. Most of the members of the society belong to the faculties of medical colleges. A report of this character presented by this society with definite recommendations and a practical outline was bound to attract wide attention and exert great influence. If physicians are to receive adequate preparation for becoming leaders in preventive pediatric work, the instruction in the medical college must be strengthened and extended. The work of this committee has been of incalculable value toward accomplishing this result.

At the 1921 meeting, a committee of three was appointed to act as an "Advisory Committee on Matters Relating to Health" and to work in conjunction with similar committees from the American Child Health Association and the American Gynecological Society. Drs. Shaw, Talbot and Ramsey were placed on this committee, and they assisted in the preparation of a plan for general education along the lines of maternal care and the prevention of stillbirths.

The 1923 meeting is memorable on account of Dr. Holt's presidential address on "American Pediatrics—A Retrospect and a Forecast." This was perhaps the last public address he delivered in this country. Howland, his colleague, student and friend, for whom we also mourn, said in a memorial address that Holt "was one of the first to seek to utilize preventive medicine, not as an auxiliary weapon, but as the most important one in the struggle against disease in the young." In this masterly address, Holt visualized three distinct type of pediatricians in the future: the research workers, the practicing pediatrician who applies the best science in the treatment of sick children in the home, hospital and dispensary, and the public health pediatrician who organizes and directs this special department in a state, city or county health board. He urged that instruction should be given to medical students by all these groups in order to fit men to enter each of these fields. To quote from his address, "the duty of the pediatrist, then, is not only to advance knowledge in all subjects related to the growth and health of children, but to see that such knowledge is applied, for of what value is our knowlege unless it is used? We must be the teachers and leaders of the public in all these matters. This field we have neglected in the past; we have left the subject of popular health education too much to the nurse, the social worker and the nutrition worker, and some of these groups, largely owing to our neglect, have gotten somewhat out of hand."

Holt was one of the founders and great leaders of the child hygiene movement in this country. The later years of his life were devoted more to preventive than to curative medicine. He retired more and more from active practice and directed his energies and his sound medical knowledge to the problems of preventive pediatrics. He was a great man and an inspired leader, and we are better for having known him and worked with him. We can best honor his memory by carrying on the work he loved as he would have wished and planned.

This society has officially conducted six investigations in the forty-one years of its existence. The subjects studied were: the use of antitoxin in the cure of diphtheria, the etiology of scurvy, an inquiry into the conditions of the child in industry, the nature and extent of anterior poliomyelitis, the prevalence and control of vulvovaginitis and the status of instruction in child hygiene in medical colleges.

The full report of these studies was published in the transactions and, coming from the leading scientific society of pediatricians, was generally accepted as authoritative and carried weight in medical circles. Our new plan provides for one or more comprehensive review at each meeting. In the past, the society has not taken advantage of its position in American pediatrics in the matter of conducting investigations and making reviews of matters of general pediatric interest. For example, no report, investigation or recommendations have been made in regard to the immunization by toxin-antitoxin for the prevention of diphtheria. Lay organizations and other medical bodies have studied the various phases of this subject, but the foremost pediatric society has been silent in what has now become a general public health problem.

I have briefly outlined the activities of this society as an organization in the field of child hygiene. The attitude and practice of the individual members along these lines should reflect those of the society. Lay organizations, national, state and local, engaged in child welfare work are numerous, for the appeal of the child strikes a note of tenderness in the hearts of all. The controlling interest and power lie in the hands of the lay members. They do not appreciate nor are they familiar with the scientific facts of health. The medical profession should guide and direct the activities of these organizations, for the physician is the best equipped and therefore the logical person to solve problems relating to health. This is especially true in regard to the pediatrician whose training and work make him familiar with the problems affecting child life. The Association for the Study and Prevention of Infant Mortality came into existence as a crystallization of a wide but unorganized sentiment demanding the protection of infancy. The first president and nine of the forty-eight original directors were members of the society. During its evolution in the past twenty years into the present American Child Health Association, five members of this society have held the office of president, and today sixteen of the sixty-seven members of the board of directors belong to the American Pediatric Society. Ten of the eleven members of the Committee on Medical Service are members of this society. This is not the place to outline the plans and accomplishments of this great organization. They are known to all.

The American Public Health Association devotes a special section to the interests of child hygiene, and at their meetings programs dealing with the various aspects of this subject are presented and discussed. This organization desires and deserves the support and active cooperation of members of the American Pediatric Society.

Several reasons have been advanced to explain why medical men do not enter actively into the work of these organizations; namely, (*a*) they are still influenced by the old traditions of medicine when physicians kept the secrets of the profession among themselves; (*b*) the

health work of these organizations was not wisely planned and was not conducted on sound scientific principles; (*c*) physicians were so engrossed in their curative work that they did not have the time to devote to general and preventive health work.

The pediatrician deals with the individual child, the child hygienist with children *en masse*. The pediatrician forms his opinions from constant observation on the reaction of different children to a given system of treatment. The consensus of such observations promulgated as the definite opinions of this society would be of invaluable aid to official and lay health organizations. We should be the clearing house for information of this nature and thus the stimulating element for further mass work. This not only would redound to our credit but eventually would react to our advantage.

Lay members of health agencies complain that physicians remain aloof from their natural place in health activities. To this indictment I feel we must plead guilty. As members of the leading pediatric society in this country we have not alone a responsibility but a direct obligation to render a distinct service to lay organizations engaged in child hygiene work. Hamill said that the pediatrician has withheld his assistance and influence so long that the lay organizations have learned to do without him.

PREVENTIVE PEDIATRICS

Child hygiene, as has been pointed out by Veeder, is a field method of applying some of our knowledge of preventive pediatrics. It deals with a group, while preventive pediatrics deals with an individual. Veeder's definition of preventive pediatrics is "Knowledge that will enable a child to be well born, to come into the world strong and healthy, to thrive lustily and without halt during infancy, to develop and grow in a normal way during childhood, to be able physically and mentally to attain a sound education, to acquire good habits of living and avoid bad ones, to avoid psychological abnormalities so that the child adjusts himself to his social environment, to pass through the difficult period of puberty and adolescence into a sound normal maturity, to prevent by scientific measures so far as we are able to infectious diseases of childhood—these are some of the aims and objects of preventive pediatrics."

Preventive pediatrics is the type of practice that should be one of the chief activities of the children's specialists of the future. It forms the major part of the office work of the pediatrician of today. Children are brought to him for thorough physical examination, preventive inoculations, advice concerning diet, clothing, home care, personal hygiene, behavior and habit problems, etc. The family physician as a rule is not qualified to do this work, nor is he interested, for until the past few years he received no instruction along these lines in his medical course.

His chief concern is with the sick, not with the well child. Largely on account of his indifference, parents turn to the children's specialist for service along these lines. The term "Specialists in Diseases of Children" is not entirely descriptive of the work of the pediatrician. This term implies only the pathogenic and ignores the healthy, normal, physiologic background. "Children's specialist" is a more comprehensive term, although the laity are now better acquainted with the meaning of the word "pediatrics" and no longer confuse it with chiropodist and the feet. The children's specialist should watch over the health and destiny of the child until puberty. The pediatrician who knows and understands his little patient in health, is acquainted with his manners and habits, his heredity and environment, has gained his affection and confidence and as a rule feels a deep sense of personal interest, affection and responsibility is the physician best qualified to treat the child if he becomes ill.

Curative and preventive pediatrics go hand in hand and should not be separated. Specialism in children should never be so finely drawn that one man looks after the child only when he is well and another when he is ill.

PEDIATRICS AND OBSTETRICS

Preventive pediatrics begins with the new-born infant who belongs to the realm of pediatrics, not of obstetrics. There are a number of hospitals in this country in which the infant passes into the service of the pediatrician as soon as he is born. This has proved so successful that it deserves to be followed more generally in private practice. Obstetrics essentially is a surgical, while pediatrics is a medical, problem. The chief interest of the obstetrician is with the mother, while that of the pediatrician—by virtue of his training, inclination and habits of thought—is with the infant. He is better fitted and educated to solve the problems of the new-born and young infant. Ready at all times, as the obstetrician must be to meet emergencies, exhausting hours, broken sleep and the "drama of the operating room," he is not likely to be as well equipped psychologically for the detailed, painstaking care which good pediatrics demands. In spite of this it is the general practice of obstetricians to assume full charge of the infant, prescribing artificial feedings and treating minor ailments for from one to nine months after birth. Some obstetricians charge a flat rate which includes prenatal and postnatal care of the mother and child, while others in the same locality have to do the same to meet the competition. The general practitioner in bygone days used to deliver the infants and look after them through infancy and childhood. The obstetrician who succeeds him assumes the responsibility of the infant as well as the mother, and it is hard for him to relinquish his hold and admit that the infant is only a by-product of obstetrics. For the best interests of the health of

the infant, the obstetrician and the pediatrician should not work independently, but should combine and cooperate. Litzenberg, an obstetrician well known to many members of this society, urged obstetricians and pediatricians "to meet on the common ground of infant welfare, to dissipate the twilight with the bright sun of mutual understanding, and to cooperate and not to clash."

The obstetrician should, of course, assume entire responsibility for all the details of prenatal care and the improvement of the mother's health, and should make a study of all the influences that may affect the unborn child. He should turn all data that can be made of assistance in the care of the infant over to the pediatrician and should consider the infant as soon as he is born a subject for his colleague and friend —the children's specialist.

There is no branch of medicine in which the preventive side has been so fully developed and practiced as in pediatrics. In his interesting history of this subject in Abt's System of Pediatrics, Garrison said "that pediatrics was elevated in the Twentieth Century from its anciliary status as a dependent dwarf of ordinary medical practice into the larger atmosphere of social or preventive medicine of which it is now one of the most important independent branches."

At the last meeting, the society authorized some radical changes in the character and preparation of the program. The importance of preventive work was recognized, and "preventive pediatrics including its social aspects" was specifically designated as one of the subjects for consideration. The question of the "teaching of pediatrics" was also one of the subjects to be included in the program of the annual meeting.

In our individual professional work, as well as in our society endeavors, let us practice what we preach and what we personally recognize as the ideal of our high calling in medicine. We are living in the dawn of a new era in the practice of medicine. Let us awake to the magnificent opportunities for service that are opening upon all sides.

TYPHOID FEVER IN CHILDREN

A STUDY OF SIXTY-SEVEN CASES *

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Recent statistics [1] reveal a definite decline in the morbidity and mortality of typhoid fever in the larger cities of the United States. This decline, together with the atypical picture that many cases of typhoid fever present, favors the possibility that typhoid fever in such cases will be overlooked unless the physician remains fortified with the knowledge of what constitutes the typical picture. In adults this is a more or less familiar and well defined clinical entity. Typhoid fever in children,[2] however, differs in some respects from typhoid fever in adults, and often the signs and symptoms presented in children may be entirely misleading.

In the four years from January, 1925, to November, 1928, inclusive, sixty-seven children ill with typhoid fever and ranging in ages from 10 months to 12 years were admitted to the pediatric ward of the Cook County Hospital. A study of the observations in their cases follows.

ANALYSIS OF CASES

Incidence.—The disease occurred in thirty-seven boys and thirty girls. One and four-tenths per cent of the cases were in children under 2 years of age, 23.7 per cent in children between the ages of 2 and 5 and 74.6 per cent in children between the ages of 6 and 12. Percy's [3] analysis of 4,717 cases of typhoid fever in children up to 12 years of age revealed an almost similar incidence according to age. The youngest patient with typhoid admitted to the Babies' Hospital in New York [4] was 8 months of age, and Griffith [5] reported cases of typhoid fever in infants 3, 5 and 9 months old, respectively. The youngest patient in this series was 10 months of age.

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* From the pediatric ward of the Cook County Hospital.

1. Typhoid Fever in the Larger Cities of the United States in 1927, J. A. M. A. **90**:1624 (May 19) 1928.

2. Usher, S. J.: A Study of 175 Cases of Typhoid Fever in Children Occurring During a Recent Epidemic in Montreal, Canad. M. A. J. **17**:1846 (Dec.) 1927.

3. Percy, in Abt, I. A.: Pediatrics, Philadelphia, W. B. Saunders Company, 1925, vol. 6, p. 12.

4. Holt, L. E.: Diseases of Infants and Children, ed. 8, New York, D. Appleton & Company, 1922, p. 1016.

5. Griffith, in Holt (footnote 4).

Symptoms.—At Onset: The first symptom of the disease occurred within seven days prior to the admission to the hospital in thirty-two, or 49 per cent of the patients in this series; within from eight to fourteen days in twenty, or 29 per cent; within from fifteen to twenty-one days in nine, or 13 per cent, and within one month in one. An abrupt onset occurred, therefore, in half of these patients. The various symptoms characterizing the onset of the disease are recorded in table 1. Headache and fever appear to have been the most frequent initial complaints. Abdominal pain ushered in the illness in almost half of the cases. Sore throat, photophobia, burning and frequency of urination and generalized

TABLE 1.—*Incidence of Symptoms Characterizing the Onset of Typhoid Fever in Children*

Symptoms	Number of Cases	Total Number of Cases	Percentage
Fever	..	54	80.5
Headache	..	53	79.1
Abdominal pain			
Vague	13		
Generalized	10		
Right lower quadrant	4		
Left lower quadrant	1		
Lower half	1		
Upper half	1		
Epigastric	1		
Umbilical	1	32	47.6
Vomiting			
With abdominal pain	11		
Without abdominal pain	8	19	28.3
Diarrhea		25	37.3
Constipation		9	13.4
Cough		24	35.8
Epistaxis		9	13.4
Sore throat		6	8.9
Chill		5	7.4
Generalized aches		5	7.4
Drowsiness		12	17.9
Anorexia		8	11.9
Malaise		6	8.9
Photophobia		3	4.4
Frequency of urination and burning		2	2.9
Rhinitis		2	2.9
Dysphagia		1	1.4

aches were other, infrequent and unusual initial symptoms. Convulsions at the onset did not occur in any patient in this series. Usher [2] recorded but one case in which there were convulsions at the onset in his study of 175 children with typhoid fever.

During the Attack: Table 2 reveals the clinical observations in these children during the course of the illness in the hospital. Enlarged spleen was clinically demonstrable in only half of the cases but this condition was noted more often than rose spots. Both signs were present most often during the second week of illness. Abdominal tenderness was present in almost a third of the patients in this series, and 25 per cent of these had this tenderness localized in the right lower quadrant. The rather abrupt onset of the disease, with the localized abdominal tenderness and fever and vomiting, so closely simulated an attack of

acute appendicitis that it was often difficult to decide whether to resort to surgical measures or to make further observation. Acute pharyngitis associated with suppurative otitis media and frequently some abdominal tenderness were the only observations early in the course of the disease in some of the children. In others, rigidity of the neck and positive Kernig and Brudzinski signs outshadowed any other observation. Such protean manifestations clearly emphasize the necessity of a familiarity with the possibilities of the disease in order that the correct diagnosis may be reached at the earliest moment.

TABLE 2.—*Incidence of the Clinical Observations Characteristic of Typhoid Fever in Children*

Symptoms	Number of Cases	Total Number of Cases	Percentage
Palpable spleen			
First week *	9		
Second week	16		
Third week	3		
Fourth week	1	34	50.7
Rose spots			
First week	9		
Second week	12		
Third week	3		
Fourth week	2	26	38.8
Abdominal tenderness			
Diffuse	9		
Right lower quadrant	5		
Right upper quadrant	2		
Left upper quadrant	1		
Lower half	1		
Epigastric	1		
Umbilical	1	20	29.8
Rigidity of neck		7	10.4
Lethargy		7	10.4
Pharyngitis		5	7.4
Sordes		4	5.9
Disorientation		3	4.4
Rhinitis		2	2.9
Bronchitis		2	2.9
Dysuria		1	1.4
Regurgitation through nose		1	1.4
Conjunctivitis, ecchymosis, vomiting, delirium		1 each	1.4

* Within seven days following the first complaint.

The pulse rate in one fourth of these patients was more rapid in proportion to the degree of fever than it usually is in adults with this disease. Pulse rates of 136 and 144 in the presence of temperatures of 101 F. and 102 F. were rather frequent. The temperature charts revealed variations and irregularities. A septic type of fever one day was frequently followed by a remittent type the next day. The average duration of fever in this series of cases was twenty days.

Laboratory Observations.—The results of the Widal test and of cultures of the blood, urine and stools for typhoid bacilli are recorded in table 3. Positive Widal reactions in dilutions of 1:1,280 were obtained in more than half of the serums tested. The highest number of positive results was obtained in the second week of illness, though 25 per cent were positive within the first week of illness. In the serums of three patients, Widal reactions were positive in dilutions of 1:160 in the

second week of illness but never became positive in higher dilutions, so that other confirmative evidence of typhoid fever had to be found in the blood, urine or stools. One patient presented an unexplainable fever of two weeks' duration with tenderness over the region of the right kidney. Repeated Widal tests and cultures of the blood, urine and stools were continually negative as regards evidence of typhoid fever. Postmortem examination disclosed the typical pathologic changes of typhoid fever. In two cases, the Widal reactions were persistently negative in all dilutions, though typhoid bacilli were repeatedly recovered from cultures of the stools and urine. Positive blood cultures numbered the same in the first and second weeks of illness, and they were obtained less often

TABLE 3.—*Incidence of the Laboratory Observations in Typhoid Fever in Children*

Observations	Total Number of Cases	Number of Cases per Week of Illness				
		First	Second	Third	Fourth	Fifth
Widal Reaction:						
Positive						
1:1,280	30	5	16	7	2	..
1:640	10	3	3	3	1	..
1:320	11	3	5	3	..	..
1:160	3	1	2	..	..	..
1:80	1	..	1	..	..	..
Negative	3	..	..	..	..	..
Not tested	9	..	..	..	..	..
Blood Cultures:						
Positive	18	6	7	3	1	1
Negative	18	6	5	4	2	1
Not done	31	..	..	..	..	..
Urine Cultures:						
Positive	11	3	3	1	3	1
Negative	41	13	19	7	1	1
Stool Cultures:						
Positive	20	5	9	2	3	1
Negative	38	12	16	7	1	2
Blood Counts (white cells)						
Below 5,000	16, or 25 per cent					
From 5,000 to 7,500	25, or 39 per cent					
From 7,500 to 10,000	8, or 12 per cent					
From 10,000 to 12,000	12, or 18 per cent					
From 12,000 to 20,000	4, or 6 per cent					

than positive Widal reactions. Cultures of the stools revealed the typhoid bacilli more often than cultures of the urine and the number of positive observations in both was highest during the second week of illness (table 4).

The specimens of urine of fifty-five patients in this series routinely examined during their stay in the hospital revealed no abnormal conditions in thirty-one, only albumin in nineteen, pus and albumin in three, blood in one and acetone in one. These observations were all only temporary. Blood was present in the stools in six cases. The blood count revealed a definite leukopenia in 76 per cent of the cases and a relative leukopenia in view of the high fever in an additional 18 per cent. In 6 per cent of the uncomplicated cases, the blood showed a leukocytosis of from 12,000 to 20,000. Spinal puncture was resorted to in ten patients with definite signs of meningeal irritation. The fluid in nine

cases was clear, with no increase in pressure or globulin, and revealed cell counts of from three to ten lymphocytes. In one case the fluid showed an increase in pressure, was slightly turbid, contained 350 cells mostly polymorphonuclears, revealed the typhoid bacilli on culture and gave a positive Widal reaction. Widal tests of the spinal fluid in three other cases gave negative results in all dilutions, and cultures were sterile.

Complications.—Twenty-two patients in this series, or 34.3 per cent, suffered complications (table 4). Suppurative processes, manifested as otitis media, abscesses, furuncles and paronychia, were relatively common. Bronchopneumonia occurred in five patients. Intestinal hemorrhage or perforation did not occur in any patient. One case of complicating myocarditis in a boy 10 years old had been under observation for three years at the time of making this report. During this time,

TABLE 4.—*Incidence of Complications in Typhoid Fever in Children*

Complications	Number of Cases	Percentage
Suppurative otitis media	6	8.9
Furunculosis	2	2.9
Abscesses	2	2.9
Paronychia	2	2.9
Bronchopneumonia	5	7.4
Pyelitis	2	2.9
Myocarditis	1	1.4
Meningitis (typhoidal)	1	1.4
Unknown, with death during convalescence	1	1.4
Total	22	34.3

he was forced to re-enter the hospital on several occasions because of decompensation. Examinations of the heart at these times revealed marked cardiac enlargement, a palpable apex beat displaced down and out to the left and regular but feeble heart tones; at no time were murmurs audible.

Prognosis.—The duration of illness, considered from the date of the first complaint to the discharge from the hospital, varied from three to ten weeks with the severity of the infection and the incidence of complications. There were nine deaths in this series. Four patients died in the second week of illness, two each in the first and third weeks and one in the tenth week. The cause of death of the latter patient during convalescence was unexplainable. Five of the patients showed signs of meningeal irritation prior to death, one having a proved case of typhoidal meningitis. Five presented evidence of bronchopneumonia either before death or at autopsy. The mortality rate in this series of sixty-seven children was 13.4 per cent.

SUMMARY

In a study of sixty-seven children ill with typhoid fever, who ranged in age from 10 months to 12 years, the following observations appear noteworthy:

1. The onset was relatively abrupt in almost one half of the cases.

2. Abdominal pain was a frequent initial complaint and, because of its location at times in the right lower quadrant and sudden onset with vomiting, it occasionally made difficult the exclusion of acute appendicitis.

3. Signs of meningeal irritation were relatively frequent, and often the disease with this complication simulated the picture of a true primary meningitis.

4. The pulse rate was rapid and in proportion to the degree of fever in one fourth of the cases.

5. The blood in 6 per cent of the cases revealed a leukocytosis in the absence of complications, instead of the usual leukopenia.

6. Positive Widal reactions outnumbered the positive blood cultures obtained, and both were more frequently obtained during the second week of illness.

7. The stools yielded a higher percentage of positive cultures than the urine.

8. Complications were largely suppurative processes.

9. Death occurred most often in the second week of illness. Signs of meningeal involvement frequently preceded death.

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CARBOHYDRATE TOLERANCE IN INFANTS AND IN YOUNG CHILDREN WITH CELIAC DISEASE*

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A study of the blood chemistry in two patients with celiac disease showed an increased tolerance for dextrose in both. A search of the literature revealed no data on carbohydrate metabolism in this disease. The question seemed of importance, and the investigations were continued until we are able to report our observations in fourteen cases.

TECHNIC

The experimental procedure described in a previous communication has been followed with but two deviations. Some of the patients were on a milk-free diet which necessitated a change in the meal preceding the test. Instead of milk and toast, the same quantity of protein carbohydrate and fat were given in the form of toast, egg and butter. In cases 1, 2, 3 and 4, the dextrose given was calculated according to the actual weight of the patient. However, all the patients studied were so much underweight that the quantity of dextrose given was small compared to that given to a normal child of the same age. In order to provide a fair basis of comparison, in all subsequent cases the dextrose given was calculated on the normal weight for the age of the patient.

Without resorting to catherization, it was not possible to obtain specimens of urine at definite time intervals. In some cases, no urine at all was obtained. The sugar in the urine was estimated qualitatively with Benedict's reagent and quantitatively by the method of Benedict and Osterberg.[1]

RESULTS

All the patients showed increased tolerance for dextrose (table 1). With one exception (case 2), the individual maximum increase in blood sugar varied between —12 and +13 mg. per hundred cubic centimeters. In the normal child the average increase is 32 mg. per hundred cubic centimeters. In case 2, one of the milder cases, there was an

* Submitted for publication, Jan. 8, 1929.

* From the Chemical Laboratory, Babies' Hospital, and the Department of Diseases of Children, College of Physicians and Surgeons, Columbia University.

1. Benedict, S. R., and Osterberg, E.: J. Biol. Chem. **48**:51, 1921.

increase of 25 mg. per hundred cubic centimeters in the blood sugar, an increase at the lower level of normal. However, in this patient the control sugar was low, 72 mg. per hundred cubic centimeters, so that even with an increase of 25 mg. the blood sugar, 97 mg. per hundred cubic centimeters, was still well within the normal limits (from 80 to 110 mg. per hundred cubic centimeters). The average control blood sugar in this series was 93 mg. per hundred cubic centimeters. One hour after the ingestion of dextrose the average blood sugar was 94 mg. per hundred cubic centimeters, while two hours after, it was 89 mg. per

TABLE 1.—*Alimentary Dextrose Tolerance in Patients with Celiac Disease* *

				Blood Sugar, Mg. per 100 Cc.			Urine		Blood		
Case	Sex	Age	Body Weight, Gm.	Control	1 Hr. after Dextrose	2 Hrs. after Dextrose	Interval Following Ingestion of Dextrose	Sugar Qualitatively	Calcium, Mg. per 100 Cc.	Phosphorus, Mg. per 100 Cc.	Nonprotein Mg. per 100 Cc.
1	M	21 mo.	8,800	93	102	99	.....	.....	....	...	48
2	F	32 mo.	11,300	72	81	97	.....	.....	10.8	4.0	....
3	M	23 mo.	6,790	66	67	67	24 hour specimen	Negative	....	...	....
4	F	16 mo.	7,400	84	88	93	.....	.....	....	...	....
5	M	16 mo.	5,900	111	112	109	½ hour 5 hours	Trace Negative	9.0	3.8	....
6	M	20 mo.	8,200	85	90	81	.....	.....	9.4	4.4	....
7	M	20 mo.	5,700	104	105	101	.....	.....	....	...	....
8	M	21 mo.	6,400	114	122	113	.....	.....	....	...	....
9	M	15 mo.	8,000	97	88	88	40 min.	Negative	....	...	....
10	F	2 yr.	7,000	87	87	100	1½ hrs. 2 hours	Negative Negative	9.3	3.4	....
11	F	21 mo.	6,900	102	100	100	5 hours 7 hours	Lost Negative	7.8	3.4	39.8
12	M	4 yr.	14,310	111	93	99	1½ hrs. 3½ hrs.	Negative Negative	8.5	4.3	25.6
13	F	2 yr.	8,600	85	85	85	5 specimens 6 hours	Negative	7.7 10.0	3.4 3.9	.... 27.8
14	M	17 mo.	7,645	107	109	105	1¾ hrs. 6 hours	Negative Negative	8.9	3.8	....

* 1.75 Gm. of dextrose per kilogram of body weight was given.

hundred cubic centimeters. This gives a blood sugar curve much flatter than that of normal infants (chart 1).

In eight cases, the urine was examined for sugar following the ingestion of dextrose (table 1). In seven there was a negative reaction with Benedict's qualitative reagent. In case 5, a specimen of urine voided one half hour after the ingestion of dextrose showed a trace of sugar qualitatively, and 0.158 per cent quantitatively. The next specimen voided five hours later showed no sugar qualitatively. However, repeated urinary examination gave no evidence of a low renal threshold in this patient (table 2). Determinations of sugar were made on five twenty-four hour specimens of urine. On one day the urine showed a trace of sugar qualitatively and 0.12 per cent quantitatively, which is

just above the normal limit. Nevertheless, the total quantity of sugar excreted, 0.39 Gm., was not pathologic. Moreover, on the other four occasions, the sugar content of the urines was normal.

Twenty-four hour specimens of urine were collected from three other patients, but unfortunately were not complete. There was, however, no evidence of glycosuria. From a fifth patient, the urine was collected and analyzed daily for five days. At no time was the amount of sugar present greater than normal (table 2).

In five patients the test was repeated one or more times in order to determine whether the tolerance for carbohydrate was consistently and constantly decreased. In all cases, flat curves were obtained (table 3).

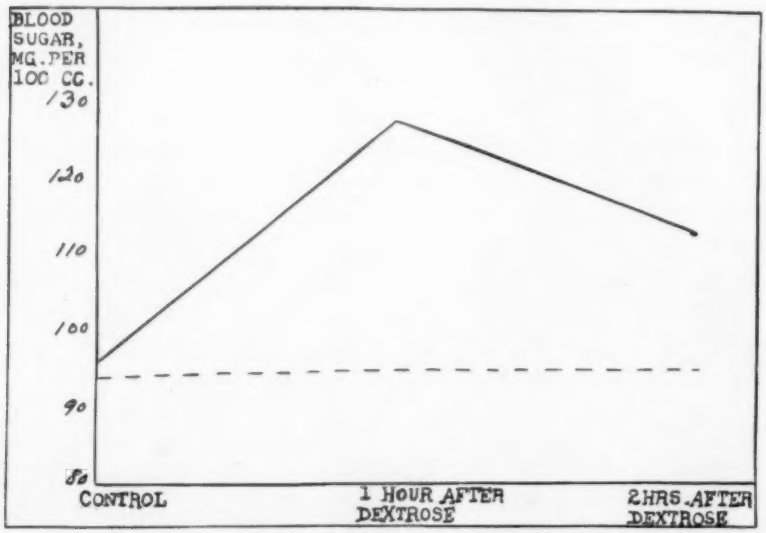

Chart 1.—Alimentary dextrose tolerance of patients with celiac disease; 1.75 Gm. of dextrose in 50 per cent solution was given per kilogram of body weight. The broken line indicates patients with celiac disease and the solid line, normal infants.

In two cases a larger amount of dextrose was given, but failed to bring about a greater increase in blood sugar (table 4).

It is known that fasting will decrease the tolerance for carbohydrates.[2] In two cases the test was done after a sixteen hour fast instead of after a four hour fast. In one case it was found that the control blood sugar was much lower after a sixteen hour fast (81 mg. per hundred cubic centimeters) than after a four hour fast (103 mg. per hundred cubic centimeters). After the ingestion of dextrose the blood sugar rose to its former level, 104 mg. per hundred cubic centimeters,

2. Du Vigneaud, V., and Karr, W. G.: J. Biol. Chem. **66**:281, 1925.

TABLE 2.—*Determination of Sugar in Twenty-Four Hour Specimens of Urine*

Case	Date	Volume, Cc.	Per Cent Sugar	Total Sugar Excreted Gm.	
3	3/ 6	50	0.019	.....	Specimen incomplete
6	12/30	90	0.089	.....	Specimen incomplete
11	10/21	130	0.057	.....	Specimen incomplete
14	1/15	200	0.054	.....	Specimen incomplete
5	5/25	410	0.035	0.143	
	5/27	21	0.120	0.028	10 a.m. to 1 p.m.
		51	0.122	0.062	1 p.m. to 6 p.m.
		80	0.126	0.108	6 p.m. to 11 p.m.
		170	0.116	0.192	11 p.m. to 8 a.m.
		331	.....	0.390	
	6/14	380	0.032	0.121	
	6/15	220	0.031	0.068	
	6/17	560	0.037	0.207	
12	10/ 6	320	0.039	0.128	
	10/ 7	460	0.032	0.147	
	10/ 8	480	0.073	0.547	Dextrose tolerance test
	10/ 9	920	0.026	0.239	
	10/10	960	0.025	0.237	

TABLE 3.—*Repetition of Dextrose Tolerance Test* *

				Blood Sugar, Mg. per 100 Cc.			Urine			
Case	Sex	Age	Body Weight, Gm.	Control	1 Hr. after Dextrose	2 Hrs. after Dextrose	Interval Following Ingestion of Dextrose	Sugar Qualitatively	Date	
5	M	16 mo.	5,900	111	112	109	½ hour	Trace	4/ 9	
							5 hours	Negative		
			5,840	102	102	102	.....	.....	6/ 2	Stomach lavage 2 hours after ingestion of dextrose; 0.719 Gm. of dextrose recovered
			5,630	81	104	103	.....	.....	5/20	Test done after 16 hour fast
10	F	2 yr.	7,060	87	87	100	½ hour	Negative	6/15	
							2 hours	Negative		
			9,075	122	128	115	.....	.....	7/25	
			8,625	105	103	106	.....	.....	8/23	
11	F	21 mo.	6,900	88	95	96	.....	.....	8/12	
				102	100	100	.....	.....	10/19	
13	F	2 yr.	8,600	85	85	85	.....	Negative	11/ 2	
			8,250	97	97	97	2 hours	Negative	12/16	
				93	94	84	.....	.....	12/24	12/23, 6 p.m., broth and vegetables. 12/24, 6 a.m., no feeding
14	M	17 mo.	7,645	107	109	105	1¾ hrs.	Negative	11/ 5	
							6 hours	Negative		
			6,280	83	96	100	1¾ hrs.	Negative	12/30	
				103	105	101	.....	.....	1/14	

* 1.75 Gm. of dextrose per kilogram of body weight was given.

and two hours after was still at that level, 103 mg. per hundred cubic centimeters. In the second case, however, no such increase in blood sugar was observed. The control blood sugar, 93 mg. per hundred cubic centimeters was no lower after a sixteen hour fast than it had been after a four hour fast on two occasions (85 and 97 mg. per hundred cubic centimeters). One hour after the ingestion of dextrose, the blood sugar was 94, and two hours after, it was 84 mg. per hundred cubic centimeters (table 3).

In order to determine whether an extremely transitory increase in blood sugar took place in one patient, the estimations of sugar were done at fifteen minute intervals for one hour following the ingestion of 30 Gm. of dextrose. The control blood sugar was 103 mg. per hundred cubic centimeters. Fifteen minutes after the ingestion of dextrose, it

TABLE 4.—*Effect of Increased Dose of Dextrose in Alimentary Dextrose Tolerance Test*

Case	Sex	Age	Body Weight, Gm.	Dextrose Given, Gm.	Blood Sugar, Mg. per 100 Cc. Control	1 Hour after Dextrose	2 Hours after Dextrose	Date	
5	M	16 mo.	5,840	17.5	102	102	102	6/ 2	
			5,825	30.0	103	104	103	6/ 5	15 min. after ingestion of dextrose, blood sugar 121 mg. per 100 cc.; 30 min after, blood sugar 124 mg. per 100 cc.; 45 min. after, blood sugar 124 mg. per 100 cc.
			5,635	50.0 33⅓% solution	103	109	84	5/ 2	Vomited 1½ hours after ingestion of dextrose
6	M	20 mo.	8,250	19.4	85	90	91	12/22	
			8,225	38.8	69	67	70	12/27	

was 121 mg. per hundred cubic centimeters, thirty minutes after 124, forty-five minutes after 124, and one hour after had dropped again to 104 mg. per hundred cubic centimeters. Two hours after, it was at the same level, 103 mg. per hundred cubic centimeters (table 4).

Stomach lavage in this patient two hours after the ingestion of 18 Gm. of dextrose returned 0.719 Gm. of dextrose, showing practically complete removal from the stomach (table 3, case 5).

The tolerance of a few of these patients to carbohydrates other than dextrose was also tested (table 5). In one case galactose elicited no increase in the blood sugar, which remained at a level of 103 mg. per hundred cubic centimeters throughout the test. However, the urine gave a ++++ reaction with Benedict's reagent. Since the tolerance for galactose in the normal person is less than that for dextrose,[3] it has

3. Foster, G. L.: J. Biol. Chem. **55**:29, 1923.

been thought that ingestion of galactose would elicit a greater increase in blood sugar than that elicited by the ingestion of dextrose. A mixture of equal parts of galactose and dextrose was next given. Here again, in the normal person [4] there is a greater increase in blood sugar than after ingestion of dextrose alone. In the patient with celiac disease, no increase in blood sugar was obtained.

Fructose was given to another patient. The control blood sugar was 81 mg. per hundred cubic centimeters. One hour after ingestion of the carbohydrate the blood sugar was again 81 mg. and two hours after, was 88 mg. per hundred cubic centimeters. Fructose may simply be another

TABLE 5.—*Tolerance of Patients with Celiac Disease to Carbohydrates Other Than Dextrose*

Case	Sex	Age	Body Weight, Gm.	Carbohydrate Given	Gm.	Blood Sugar, Mg. per 100 cc. Control	1 Hr. after Dextrose	2 Hrs. after Dextrose		
5	M	16 mo.	5,900	Dextrose	18	111	112	109	4/ 9	
			5,650	Galactose	18	103	103	103	4/17	Urine sugar qualitatively ++++
			5,610	Dextrose / Galactose	15 / 15	103	103	103	5/ 8	78 per cent solution
6	M	23 mo.	8,250	Dextrose	19.4	85	90	91	12/22	
			8,050	Fructose	19.3	81	81	88	12/24	
11	F	21 mo.	6,900	Dextrose	19.4	102	100	100	10/19	
				Dextrose / Fructose	9.5 / 9.5	92	115	95	11/18	Urine for 7 hours following ingestion of carbohydrate negative for sugar
13	F	2 yr.	8,600	Dextrose	20.0	85	85	85	11/ 2	Urine for 6 hours following ingestion of dextrose negative for sugar
				Dextrose / Fructose	9.5 / 9.5	82	108	89	11/18	Urine for 7 hours following ingestion of carbohydrate negative for sugar

sugar to which the patient with celiac disease manifests increased tolerance, or it may be evidence of normal function of the liver.[5]

It is known that patients with celiac disease tolerate bananas well.[6] The carbohydrate in ripe bananas is invert sugar. Two patients were given a mixture of equal parts of dextrose and fructose, the total quantity being equal in amount to that of dextrose given in the preliminary test. In both cases, there was a definite increase in blood sugar. In one case the initial blood sugar was 92 mg. per hundred cubic centimeters; one hour after ingestion of carbohydrate it increased to 115 mg.,

4. Bodansky, M.: J. Biol. Chem. **56**:387, 1923.

5. Strauss, H.: Deutsche med. Wchnschr. **27**:757, 1901.

6. Haas, S. V.: Value of Banana in Treatment of Celiac Disease, Am. J. Dis. Child. **28**:421 (Oct.) 1924.

and in two hours dropped again to 95 mg. per hundred cubic centimeters. In the second case the control blood sugar was 82 mg. per hundred cubic centimeters, reached 108 mg. one hour after ingestion of the carbohydrate, and in two hours attained 89 mg. per hundred cubic centimeters, practically its former level. These curves would seem to indicate a more normal metabolism of invert sugar than of dextrose, and perhaps explains why patients with celiac disease do well on a diet rich in bananas.

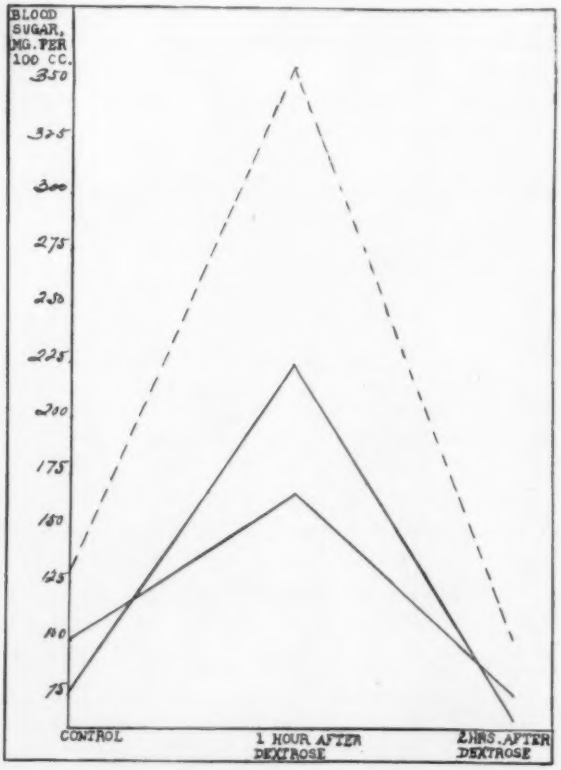

Chart 2.—Blood sugar curves following injection of 20 per cent dextrose solution—20 cc. per pound of body weight. The broken line indicates the control case and the solid line, patients with celiac disease.

In two cases the tolerance to dextrose administered parenterally was tested. Twenty per cent dextrose was given intravenously, 10 cc. for each pound of body weight. Tisdall, Drake and Brown [7] found in a series of normal infants that the average initial sugar was 85 mg. per

7. Tisdall, F. F.; Drake, C. H., and Brown, A.: Carbohydrate Metabolism of Normal Infant, Am. J. Dis. Child. **30**:675 (Nov.) 1925.

hundred cubic centimeters. One hour after the injection of the dextrose the blood sugar was 358 mg. per hundred cubic centimeters, and two hours after, it had returned to normal, 95 mg. per hundred cubic centimeters. In only one case have control experiments been done thus far, but the figures agree well with those given by Tisdall, Drake and Brown. In the two cases of celiac disease, the curves obtained were somewhat flatter (chart 2).

COMMENT

The flat blood sugar curve found after ingestion of carbohydrate in patients with celiac disease must be explained in one of three ways: a low renal threshold for carbohydrate, lack of absorption of carbohydrate from the intestines or an endocrine dyscrasia.

A low renal threshold has been fairly well ruled out in these cases. In only one patient of eight examined was sugar found in the urine following ingestion of dextrose. However, on repeated examinations of twenty-four hour specimens of urine from this patient, there was no evidence of renal glycosuria.

The large frothy stools characteristic of this disease would certainly suggest lack of absorption of dextrose as an etiologic factor in the flat blood sugar curve. There are several facts, however, which do not fit in with this theory. When the blood sugar was estimated at fifteen minute intervals following the ingestion of dextrose, an increase in blood sugar was observed during the first hour, proving that some sugar was absorbed. When galactose was given hourly, the blood sugar showed no increase, but we know that some sugar must have been absorbed because examination of the urine showed a ++++ reduction with Benedict's reagent. Moreover, an increase in blood sugar was obtained in one case when the dextrose was given after a sixteen hour fast instead of a four hour fast, again indicating some absorption from the intestines.

Whether or not lack of absorption from the intestine explains the flat blood sugar curve can be definitely decided only by determining the fate of dextrose parenterally administered. Subcutaneous injections of dextrose were tried first but, owing to marked variations in the time required for injection and absorption, proved difficult to standardize. Intravenous injection of dextrose was then resorted to.

This phase of the problem is now being studied. In two patients who received dextrose intravenously, the blood sugar curve obtained was flatter than that of a control case and that given in the literature for normal children. The weight of evidence thus far accumulated is slightly against lack of absorption as an explanation of the flat blood sugar curve.

Is there an increased tolerance for dextrose dependent on an endocrine disturbance? Herter [8] suggested the possibility of pituitary insufficiency. Still [9] reported good results in a patient treated with polyglandular extracts who in a short time was able to take an ordinary diet in place of the restricted special one and who grew with remarkable rapidity.

There is some similarity clinically between celiac disease and Addison's disease. Asthenia, lack of muscle tone, emotional instability, and capricious appetite are common to both. The gastro-intestinal symptoms are similar. Bronzing of the skin is characteristic of Addison's disease, and in some of the severer forms of celiac disease pigmentation of the skin has been observed. Moreover, in Addison's disease there is an increased tolerance to dextrose. This clinical analogy directs attention to the suprarenal glands in celiac disease.

Ryle [10] pointed out the resemblance between sprue and celiac disease. In both are found abdominal enlargement, characteristic stools and tetany as a frequent complication. This author expressed the belief that an inflammatory occlusion of some part of the lacteal system may possibly account for the common symptoms in these diseases. Scott [11] suggested the possibility of calcium deficiency in sprue and reported striking recoveries in a few patients treated with calcium lactate and parathyroid hormone. The blood calcium in his cases was little, if at all, diminished except in the late stages or in severe cases.

Tetany is a frequent complication in celiac disease and was observed in two of our cases (3 and 11). This suggests a change in calcium metabolism and in the parathyroid glands. Just how these glands influence calcium metabolism is open to question, but without doubt there is some close interrelationship. The subject of carbohydrate metabolism and the parathyroid glands is even more indefinite. In parathyroidectomized dogs, decreased tolerance for carbohydrates has been found following the oral administration of dextrose [12] and the injection of epinephrine.[13] However, these results have not been duplicated in human tetany. On injection of epinephrine, no glycosuria was observed.[14] Moreover, in this laboratory increased tolerance for dextrose was found in a number of patients with tetany (six of ten

8. Herter, C.: Infantilism from Chronic Intestinal Infection, New York, 1908.

9. Still, G. F.: Lancet **2**:229, 1918.

10. Ryle, J. A.: Guy's Hosp. Rep. **74**:1, 1924.

11. Scott, H. H.: Proc. Roy. Soc. Med., Sec. Trop. Dis. **17**:11, 1924.

12. Salvesen, H. A.: J. Biol. Chem. **56**:443, 1923.

13. Eppinger; Walter, W., and Rudinger, C., cited by Chrobac, R., and Bergmeister, O.: Wein. klin. Wchnschr. **21**:241, 1908.

14. Falta, W., and Kahn, F.: Ztschr. f. klin. Med. **74**:108, 1911.

cases studied). Parathyroid hormone itself seems to have no effect on sugar metabolism but when given before insulin, increases the hypoglycemic effect. It has been found that from one third to one fourth of the usual dose of insulin will produce convulsions in rabbits if preceded by an injection of parathyroid hormone.[15] It would be interesting to observe the effect of parathyroid hormone in celiac disease.

SUMMARY

1. Fourteen patients with celiac disease showed increased tolerance for dextrose.

2. Larger amounts of dextrose, galactose, dextrose and galactose, and fructose failed to elicit an increase in blood sugar.

3. After the ingestion of fructose and dextrose given in equal proportions, blood sugar curves were obtained similar to those of normal children following the ingestion of dextrose. This suggests a more normal metabolism of invert sugar and is a possible explanation of the celiac patient's tolerance of bananas.

4. Of the three possible explanations of this flat sugar curve, the first, a lowered renal threshold, has been disproved, and may be disregarded. Against the second, lack of absorption of carbohydrate from the intestine, there is some rather suggestive evidence, but before a definite statement can be made more experimental data are required. At the present stage of this study, the third explanation, endocrine involvement, is not untenable.

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15. Winter, L. B., and Smith, W. J.: J. Physiol. **58**:108, 1923.

THE MORO EMBRACE REFLEX IN INFANCY

ITS INCIDENCE AND SIGNIFICANCE *

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Reflexes are divided by Pavlov [1] into two main groups, conditioned and unconditioned. The unconditioned, so designated because of their independence of, or slight dependence on, surrounding conditions, are those reflexes which are transmitted by heredity and which are characteristic of the species rather than of the individual animal itself. They appear in every member of the species provided the central nervous system is normal. They may disappear with age or appear only in maturity, but they are certain to reappear in the next generation and follow a similar course.

Reflexes which are present during the first few months and which may be traced back to developmental attributes are the Moro embrace reflex, the fear reflex, the sleeping attitude and the hand reflex. The embrace reflex was first described by Moro in 1918.[2] He found that on placing an infant on a table and then forcibly striking the table on either side of the child, a motor reaction is obtained. The arms are suddenly thrown out in an embrace attitude, describing an arc and tending to approach one another with a slight tremor; the fingers are at first spread and then closed. Similar movements are observed in the lower extremities.

In explaining this reaction on the basis of an atavistic attribute, Moro referred to the observations of Doflein.[3] The latter grouped animals into four classes depending on the peculiarities associated with nourishment: 1. Pouch or marsupial nurslings which are retained in a maternal pouch during the nursing period, e.g., kangaroo and opossum. 2. Nest nurslings which are born blind and are kept for several weeks in a bed or couch previously prepared by the mother, e.g., rabbit and kitten. 3. Running-about nurslings which are fully developed on delivery but run about almost immediately after birth and take vegetables in addition to the breast, e.g., guinea-pig and horse. 4. Breast-fed nurslings who are fully developed at birth but depend on the mother for nutrition, e.g.,

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1. Pavlov: Ergebn. d. Physiol. **11**:345, 1910; quoted by Evans, C. L.: Recent Advances in Physiology, Philadelphia, P. Blakiston's Son & Company, 1926, p. 328.
2. Moro, E.: Das erste Trimenon, München. med. Wchnschr. **42**:1147, 1918.
3. Doflein, F., quoted by Moro (footnote 2).

monkey, man and bat. The motor capacities of the breast-fed nurslings, however, are not fully developed, and the infants are accordingly carried about by their mothers. In clinging to the body of the mother and in nursing, the infant assumes an embrace attitude.

Freudenberg [4] continued the studies on the Moro reflex. According to him, the reflex may be released by a heterogeneous variety of stimuli which may be grouped as follows: 1. The change of position of various parts of the body, independent of the absolute position; it is not the new position but the sudden change which produces the reflex. The position in which the child is held is of no importance provided it is physically able to perform the reaction. The reflex may be released by lifting the child without supporting the head or by holding the body with one hand and the head with the other followed by a severe jolt. The reaction is not elicited by simple ventral flexion of the head with the body in the supine position. 2. Jolting and shaking of various parts of the body, such as that produced by striking the table on either side of the infant, will invoke an immediate reaction. Passive and active movements of the child which tend toward a shaking of the head will also release the reflex. A slight tap on the abdomen may elicit it. 3. Thermal stimuli, hot or cold, will release the reflex if sufficient surface is exposed. Neither aural nor optical stimuli will produce it. The injection of hot or cold water into the ear has no effect. 4. Hiccuping may release the reflex.

The embrace reflex was found to be a normal phenomenon in infants up to the age of 3 months by both Moro and Freudenberg.[4] Schaltenbrand [5] stated that the reflex disappears between the fourth and sixth months of life. In rare instances, it may be present during the second half of the first year. Peiper and Isbert [6] found it to be present during the first four months, diminishing in intensity from then on until the eighth month. They did not obtain any positive reaction during the last quarter of the first year.

Peiper [7] called attention to a similar reaction in children above the age of 1 year. The child is placed on the observer's lap and then suddenly released from the latter's hold. The hands are immediately stretched out in an attempt to break the fall or else to right himself. Peiper considered this a residual Moro reflex. It seems to me that it may also be an expression of the fear reflex.

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4. Freudenberg, E.: Der Morosche Umklammerungsreflex und das Brudzinskische Nackenzeichen als Reflexe des Saüglingsalters, München. med. Wchnschr. **68**:1646, 1921.

5. Schaltenbrand, G.: Normale Bewegungs- und Lagereaktionen bei Kindern, Deutsche Ztschr. f. Nervenh. **87**:23, 1925.

6. Peiper, A., and Isbert, H.: Ueber die Korperstellung des Saüglings, Jahrb. f. Kinderh. **115**:142, 1927.

7. Peiper, A.: Die Hirntätigkeit des Saüglings, Ergebn. d. inn. Med. u. Kinderh. **33**:504, 1928.

In common with other atavistic reflexes, the Moro reflex is inhibited and hindered by the brain. In persons in whom the function of the brain is subnormal, the cerebral inhibitory power is lost and the reflex persists. Both Moro [8] and Freudenberg [4] expressed the belief that a positive embrace reflex subsequent to the sixth month is indicative of mental retardation or cerebral injury. They explained it on the basis of maldevelopment of the pallidal area and pyramidal tracts. Persistence of the embrace reflex has been observed by these authors in mongolian idiocy, spastic paraplegia, microcephalic idiocy and in the terminal stages of meningitis.

SCOPE AND RESULTS OF PRESENT INVESTIGATION

The object of the present investigation was the study of the Moro embrace reflex in infancy under normal and pathologic conditions. Observations were made on 300 normal and on 21 abnormal infants. They were carried out in the nursery of the United Israel Zion Hospital for the first ten days of life, in the infant feeding clinic and in private practice. When possible, the infants were followed for a period of five months or until the reflex disappeared. The abnormal children were studied in the Endocrine Clinic of the Long Island College Hospital.

The method employed in releasing the reflex was that as originally described by Moro which I had the privilege of observing during the course of a recent visit at the University of Heidelberg. An infant is placed on a table and the latter is forcibly struck on either side of the infant. In the present investigation, I have found it convenient to divide arbitrarily the response into three groups depending on the intensity of the reaction and designated as 1, 2 and 3 plus. In group 1, there is a shrugging of the shoulders, a tautening of the shoulder muscles and a slight forward movement of the arms with a flexion at the elbows. In group 2, the arms show a tendency to approach one another, the fingers are stretched and the elbows bent, but the arms do not completely describe an arc. In group 3, the complete reaction is obtained forcibly and an arc is described; there is a slight tremor of the hands, a temporary separation of the lower limbs and a stretching of the legs. The movements in the upper extremities are much more pronounced than those in the lower.

Reference to table 1 will show the incidence of the embrace reflex. The stronger reactions are found with more regularity during the first two months of life, less during the third and still less during the fourth month. I did not obtain a single instance of a pronounced 3 plus reaction during the fifth month. Every child gave some response during

8. Moro, E.: Zur Persistenz des Umklammerungsreflexes bei Kindern mit zerebralen Entwicklungshemmungen, München. med. Wchnschr. **12**:360, 1920.

the first two months. The weak reaction (1 plus) was found just as frequently during the first as during the third month. Only thirteen of the sixty-three infants examined during the third month failed to respond as against fifty of sixty-three during the fourth month. Seven

TABLE 1.—*Incidence and Intensity of Moro Embrace Reflex During the First Five Months of Life*

Month	Positive			Negative	Total
	3 Plus	2 Plus	1 Plus		
First	50	24	11	0	85
Second	50	25	6	0	81
Third	16	20	14	13	63
Fourth	3	7	3	50	63
Fifth	0	1	0	7	8
Total	119	77	34	70	300

TABLE 2.—*Intensity of Moro Embrace Reflex in Individual Infants Followed for Several Months*

Case	First Month	Second Month	Third Month	Fourth Month	Fifth Month
1	3 +	2 +	1 +	0	..
2	3 +	2 +	0	..	..
3	3 +	3 +	1 +	0	..
4	Crying	3 +	2 +	0	..
5	3 +	3 +	0	..	..
6	3 +	3 +	2 +	0	..
7	....	3 +	3 +	0	..
8	....	2 +	2 +	0	..
9	1 +	2 +	0	..	..
10	....	1 +	1 +	0	..
11	....	3 +	3 +	0	..
12	....	2 +	2 +	0	..
13	Crying	1 +	....	0	..
14	3 +	3 +	2 +	0	..
15	1 +	2 +	1 +	0	..
16	3 +	2 +	1 +	0	..
17	3 +	3 +	3 +	2 +	0 (premature)
18	3 +	3 +	0	..	..
19	....	3 +	2 +	0	..
20	3 +	3 +	3 +	0	..
21	3 +	3 +	0	..	..
22	3 +	3 +	2 +	0	..
23	....	1 +	0	..	..
24	2 +	2 +	0	..	..
25	3 +	1 +	0	..	..
26	3 +	3 +	0	..	..
27	1 +	2 +	3 +	0	..
28	....	2 +	1 +	0	..
29	1 +	2 +	....	2 +	0
30	3 +	3 +	0	..	..
31	Crying	3 +	....	0	..
32	3 + crying	2 +	2 +	0	..
33	....	3 +	3 +	0	..
34	1 +	2 +	3 +	0	..
35	3 +	2 +	1 +	0	..

of eight infants gave no reaction during the fifth month. The Moro reflex is strongest during the first two months of life and gradually diminishes in intensity from then on, disappearing at the end of the fourth month. It may be observed occasionally during the fifth month in normal infants. In two instances, the response was greater during the later than during the earlier months (cases 27 and 34, table 2).

The incidence in the new-born infant is seen in table 3. Forty-seven of fifty-four infants tested during the first ten days of life gave either a 1 or a 2 plus reaction; twenty-one of the reactions were obtained on the first day of life.

The intensity of the reaction seems to be influenced by the general condition of the child. In two infants with cerebral hemorrhage, a plus 1 response was released on the first and second days; with improvement in the general condition, however, the reflex became stronger. In a third infant with intracranial hemorrhage, a weak response was obtained on the second day. There was no change in the intensity of the reaction until three weeks later when it showed a 2 plus response. By this time the child had improved enough to be discharged from the hospital. Another infant with intracranial hemorrhage and a resulting spastic paraplegia did not give any response until the age of 6 weeks.

TABLE 3.—*Incidence and Intensity of Moro Embrace Reflex in New-Born Infants*

Days	Positive			Negative	Total
	3 Plus	2 Plus	1 Plus		
First	11	10	3	0	24
Second	2	0	0	0	2
Third	1	0	0	0	1
Fourth	1	0	1	0	2
Fifth	0	0	0	0	0
Sixth	1	2	1	0	4
Seventh	0	1	1	0	2
Eighth	1	0	0	0	1
Ninth	1	0	0	0	1
Tenth	8	8	1	0	17
Total	21	21	7	0	54

These observations are in accord with those of Peiper and Isbert [6] who expressed the belief that in sick children the muscle tone and reflex stimulation are lowered. The reflex returns when the general tone improves.

The Moro reflex is symmetrical, as pointed out by Freudenberg.[4] This tendency is so marked that there is an attempt at the embrace attitude even if one arm is held down. It may be asymmetrical, however, under the influence of asymmetrical conditions. I had an opportunity to observe four infants with unilateral brachial palsy. The reflex was released on the normal but not on the affected side. Improvement in the palsy is accompanied by a gradual increasing response on the affected side as evidenced in one child who was observed for several months. I think that absence of the embrace reflex on one side is an indication of either motor paralysis or injury on that side.

The fear reflex simulates the Moro embrace reflex in the expression of response. The arms are extended forward, the elbows bent and the fingers are at first stretched and then closed. This attitude is assumed

in crying, the child's expression of fear. In attempting the elicitation of the Moro reflex on infants during a crying spell, it was noted that, as a rule, there was no increase in the embrace attitude already present. In some instances, however, I was able to elicit the Moro reflex simultaneously with the crying. At other times, while it appeared that a synchronous expression of both reflexes had been obtained, there seemed to be an almost imperceptible pause between the time of the fear reflex and that of the Moro reflex. The latter observation is in harmony with that of Peiper [9] who thinks that it is not possible to obtain a simultaneous release of both fear and Moro reflexes. While it may apparently appear to be simultaneous, there is a momentary pause between the individual responses.

The Moro reflex was also studied in thirteen abnormal children above the age of 6 months. In accord with the observations of others,[10]

TABLE 4.—*Conditions in Which a Persistence of Moro Reflex Occurred*

Disease	Age, Months	Intensity of Reaction
Spastic paraplegia	6	3 plus
	13	2 plus
	18	1 plus
	20	1 plus
Spastic diplegia and microcephalus	16	2 plus
Hydrocephalus	6	3 plus
Hydrocephalic idiocy	12	3 plus
	16	1 plus
Mongolian idiocy	6	2 plus
	8	2 plus
	12	2 plus
	15	2 plus
Terminal stage of meningitis (streptococcic)	6	3 plus

table 4 demonstrates that the reflex persists in children with mental retardation and with disorders of the cerebral and pyramidal tracts. Improvement in either the physical or the mental deficiency is accompanied by a diminution in the intensity of the response, as exemplified in a boy, aged 12 months, who was suffering from hydrocephalus and mental retardation. A 3 plus reaction was elicited on the first examination. Four months of thyroid extract therapy resulted in some improvement in the physical deficiency as evidenced by an ability to hold the head erect. The mentality of the child was not changed. The Moro reaction at the end of the four months was 1 plus. The oldest child in whom a positive Moro reflex was obtained was 20 months and was suffering from a spastic paraplegia with mental deficiency.

9. Peiper, A.: Die Hirntätigkeit des Neugeborenen, Jahrb. f. Kinderh. **111:** 290, 1926.

10. Freudenberg (footnote 4). Moro (footnote 8).

COMMENT

Magnus [11] and de Kleijn [12] have shown experimentally that the posture of higher animals, including man, is governed by reflex action. Magnus [11] recognized several reflexes, the most important of which are the following:

The Reflex of Standing: In order to prevent the body from falling to the ground through the action of gravity, it is necessary for a group of muscles to act by reflex action against gravity.

Distribution: The normal distribution of tone is under the control of another group of reflexes.

Attitude: Different parts of the body must harmonize with one another. If one part is displaced, another must also change its position.

Righting Function: If by its own action or by some outward force, the body of an animal is brought out of its original posture, a series of reflexes are evoked whereby the original posture is again reached.

The main centers for these functions are in the subcortical brain stem. Those influencing posture are: 1. The labyrinth, which is a double sense organ. The otoliths react to change in position, and the ampullae of the semicircular canals react to acceleration. 2. The proprioceptive sense organs, which are in the muscles, joints and tendons. 3. The exteroceptive nerve endings of the body surface, chiefly the pressure sense organs which are stimulated when the body touches the ground. 4. The teleceptors which react to distant stimuli, such as the eye, ear and nose.

Besides the medulla and the midbrain, there are other parts of the body which probably have an influence on posture. Moro [2] considered that the embrace reflex is a pallidum reflex similar to one found to be highly developed in monkeys. After the age of 3 months it diminishes in intensity and ultimately disappears following the development of surrounding structures, such as the pyramidal tract.

Magnus,[11] on the other hand, stated that "neither extirpation nor stimulation of basal ganglia have given any evidence of postural influence arising in the striatum or pallidum. Our knowledge of the rôle which these centers play in the maintenance of posture is at most very restricted." He also stated that a single function or reflex is not known which is positively connected with the cerebellum in such a way that it is absent after cerebellar extirpation.

In infancy and under certain pathologic conditions, especially if there is a disturbed cerebral function, the attitudinal reflexes are released.

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11. Magnus, R.: Croonian Lecture on Animal Posture, Proc. Roy. Soc., London **98:** (Sect. B) 339, 1925.

12. De Kleijn, A.: Experimental Physiology of the Labyrinth, J. Laryng. & Otol. **38:**646, 1923.

According to Peiper,[7] the presence of attitudinal reflexes may be explained on several bases: 1. The centers and tracts which later inhibit are not as yet efficient. 2. They themselves or the receptive organs are damaged by traumatic birth hemorrhages. 3. Through a poor general condition of the child, the inhibiting tracts and centers are ineffective and the reflex stimulation is impaired, but the deeper reflexes are still present. My observations are in accord with those of Peiper, with the modification that in recent cases of cerebral hemorrhage I found a negative Moro embrace reflex. This may be explained on the basis of an incomplete development of the inhibitory powers of the brain at this age in addition to a poor general condition of the infant.

Peiper and Isbert[6] placed the Moro reflex under the group of labyrinthine reflexes and considered that the stimuli are set forth in the semicircular canals. Freudenberg[4] did not grant the relationship between the Magnus labyrinthine reflex and the Moro embrace reflex, recognizing several points of difference between them. The labyrinthine reflex depends on positions of the body so far as the position of maximum and minimum reactions is concerned. In this reflex the position of the body is the stimulus, while in the Moro embrace reflex, it is the change of position that is the important factor. If the stimulus is applied slowly, the labyrinthine reflex is increased as against a diminution or even a disappearance of the embrace reaction. A large number of stimuli which release the Magnus labyrinthine reflex have no influence on the Moro reflex. The expression of the two reflexes is different. The Moro reflex is a sudden and quickly passing motor phenomenon to which a muscle tone component is attached. It does not consist of a continuous change in muscle position as obtains in the labyrinthine reflex.

SUMMARY AND CONCLUSIONS

The Moro embrace reflex was studied in 300 normal infants and in 21 sick children presenting various pathologic conditions, such as intracranial hemorrhage of the new-born infant, brachial palsy, cerebral spastic paraplegia, monogolian idiocy, hydrocephalus, mental retardation, microcephalus and meningitis. The reflex was released by placing the infant on a table and then forcibly striking the table on either side of the infant. The arms are suddenly thrown out in an embrace attitude, describing an arc and tending to approach one another with a slight tremor of the hands; the fingers are at first spread and then closed. Similar but less intensive movements are observed in the lower extremities.

I have found it convenient to divide arbitrarily the response into three groups depending on the severity of the reaction. The Moro reflex is an unconditional reflex which is strongest during the first two months of life, diminishing in intensity from then on and disappearing at the

end of the fourth month. It may be observed occasionally during the fifth month in normal infants. It is a symmetrical reflex, and absence on one side indicates either motor paralysis or injury on that side. Severe cerebral injury and general weakness diminish the intensity of the response during the first few weeks. There is an increased intensity with general improvement. Persistence of the Moro reflex in children above the age of 6 months signifies injury of the cerebral or the pyramidal tract.

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COMPARATIVE EFFECTS OF DIPHTHERIA TOXOID AND TOXIN-ANTITOXIN AS IMMUNIZING AGENTS *

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The value of diphtheria toxoid (anatoxin-Ramon), the modified toxin of diphtheria, in active immunization of man has been firmly established since Glenny's experiments with animals and Ramon's clinical demonstration of its efficiency. Its use on a broad scale has grown, particularly in France and in Canada. The lack of any extensive trial of toxoid in this country is, to a large extent, attributable to the strong foothold that prophylaxis with toxin-antitoxin has gained, following the impetus given to its popularization by Park and his collaborators. Through their laudable efforts, a marked reduction in the incidence of diphtheria has been effected in this country.

The preference that toxoid has received in other countries within the last few years is the result of certain important advantages that have been recognized in the use of this material. These advantages have been emphasized by Ramon and Helie [1] in a recent report to the American medical profession, summarizing the experiences with toxoid. It is our purpose in this communication to report observations on the use of toxoid in a well controlled group of adults and also to explain, if possible, certain interesting phenomena incidental to its use.

Many years ago, Ehrlich and others noted that diphtheria toxin solutions undergo deterioration with time and tend to lose their toxicity, retaining, however, their original power of neutralizing antitoxin. It has also been known for many years that a similar modification can be brought about by solution of formaldehyde. As early as 1904, these toxoid solutions were used in the immunization of horses for the routine production of antitoxin. Glenny and Hopkins,[2] studying the effects of such a modified toxin, found this material to be of definite value as an immunizing agent. Using a concentrated form of toxoid,

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1. Ramon, G., and Helie, I. G.: Diphtheria Prophylaxis in France, J. A. M. A. **91**:1028 (Oct. 6) 1928.

2. Glenny, A. T., and Hopkins, B. E.: Brit. J. Exper. Path. **4**:283, 1923.

Glenny, Hopkins and Pope [3] were able to detect antitoxin in the blood of a normal rabbit nine days after injection and, further, found that guinea-pigs gave negative reactions to the Schick test in eleven days after this treatment. Ramon [4] perfected the method of preparing toxoid by developing a procedure that renders the material completely atoxic and at the same time retains its antigenic properties. He found its intrinsic immunizing value to be definitely measurable by the phenomenon of flocculation,[5] which consists of the interaction of the specific toxin and antitoxin in vitro.

The toxoid material employed in our experiments is a recently recognized [6] commercial product. In its preparation the diphtheria toxin [7] is obtained in the usual manner by growing a virulent strain of diphtheria bacillus in veal broth, fermented with *B. coli* and treated with Witte's peptone. At the end of a week, the diphtheria toxin is filtered and the filtrate treated with 3 cc. solution of formaldehyde per liter. The toxin is then placed in an incubator at a temperature of about 40 C. and is kept there until 5 cc. no longer kills a guinea-pig weighing 300 Gm. Thus, detoxification is brought about by the addition of solution of formaldehyde and prolonged heating. The completeness of the detoxification is determined by removing samples and testing from time to time. When this point is attained, the material is tested for its immunizing value by injecting graduated doses of the material into a large series of guinea-pigs. At the end of one month, each of these guinea-pigs receives five fatal doses of standard diphtheria toxin. That dose which protects 80 per cent of the guinea-pigs against this amount of toxin has been found to be a sufficient dose for human immunization. The toxoid is then diluted until this amount is contained in 1 cc. The diluted material constitutes the market product.

It has been pointed out [1] that toxoid retains its antigenic power and remains free from any traces of toxicity, the substance being particularly resistant to heat. The stability of its antigenic power, its innocuousness and its resistance to heat make it an ideal material for use on a broad scale.

The Schick test has been employed as a simple means of determining the production of immunity following the administration of toxin-antitoxin mixtures and toxoid. Because of its frequent application in this respect, it seemed important for us to recognize any possible source of error arising from faulty technic and from the use of solutions which are not freshly prepared. The possibility of error in this direc-

3. Glenny, A. T.; Hopkins, B. E., and Pope, C. G.: J. Path. & Bact. **24**:261, 1924.

4. Ramon, G.: Compt. rend. Soc. de biol. **86**:661, 1922; **86**:771, 1922; **86**:813, 1922; **87**:167, 1923.

5. Ramon, G.: Ann. de l'inst. Pasteur **38**:1, 1924.

6. Report of Council on Pharmacy and Chemistry, J. A. M. A. **91**:321 (Aug. 4) 1928.

7. Personal communication of the manufacturer.

tion was emphasized by Park.[8] In performing our Schick tests, then, we were solicitous of our technic and were careful to use only toxin that was well within the expiration date. We were particularly impressed by the possibility of misinterpretation due to errors from this source. From a review of the histories of several classes of student nurses on whom Schick tests had been performed before and after an interval of from one to three years, we found that of a group of 124 there were 64 who gave negative reactions to the original test, while on the retest 21, or 33 per cent, of these 64 showed positive reactions. We could only explain this discrepancy as being due to either faulty technic, the use of impotent toxin, or both.

We had further ample proof of the possible inaccuracies that may arise in the employment of the Schick test. There was at our disposal a group of twelve nurses, whom we found gave definitely positive reactions to this test, but whom an independent worker had previously found to give negative reactions. Of these twelve persons, seven were given two 1 cc. doses of toxoid, and the remaining five were untreated. Seven months later the seven who were treated gave negative reactions, whereas in the five controls the reactions remained positive. The third or final testing was made one year after the original test, thus eliminating the possibility of a seasonal variation.

A control test was performed on all the patients studied in our investigation. The importance of performing a control test lies primarily in the detection of pseudoreactions to the Schick test, which, it has been pointed out, seem to bear some definite relation to a previous sensitization: either to some specific product of the diphtheria bacillus [9] or a sensitization to a protein in the material (e. g., protein from the veal broth). As others [10] have noted, we have also observed that the pseudoreaction to the heated toxin may persist for some time and frequently may show the same degree of reaction and may go through the same evolutionary pigment and desquamative changes as the reaction to the unheated toxin itself.

Our study was made on groups of nurses and medical students, most of whom came from small towns or rural communities. In all, 291 were tested; of these, 212, or 73 per cent, were found to give positive reactions; 59, or 20 per cent, gave negative reactions, and 20, or 7 per cent showed pseudoreactions. The high incidence of positive Schick reactions in our group is interesting when compared with the

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8. Park, W. H.: Active Immunization Against Diphtheria, Am. J. Dis. Child. **32**:709 (Nov.) 1926.

9. Dudley, S. F.: Medical Research Council, Special Report Series, 1923, no. 75.

10. Hertz, P.: Ugesk. f. Laeger. **33**:612, 1924.

25 per cent incidence in Park's [11] series of subjects from 10 to 20 years of age and 20 per cent in those over 20 years. This variance can be explained by the fact that our subjects, in contradistinction to those of Parks, came from the country districts where the opportunity for the development of a natural immunity is not so great. Zingher [12] recorded similar observations in nurses coming from rural districts, from 50 to 75 per cent of his subjects showing a positive reaction.

A group such as ours constitutes an ideal one for the clinical determination of the intrinsic antigenic value of any immunizing agent, for, as Glenny [13] has pointed out, "the true test of any type of antigen would be the rate at which it immunizes the Schick reactors in a population with a very high positive rate." This statement derives support from his experiments on animals, in which he has shown that the primary stimulus does not produce a permanently appreciable quantity of antitoxin in the blood, but that when a secondary stimulus or immunizing agent has been received, the tissues are prepared for a prolific produc-

TABLE 1.—*Results with Toxoid*

		Number Rendered Negative to Schick Test	Per Cent
Number of persons giving positive reactions to Schick test treated	104		
Number receiving 2 doses (1 cc. each)	89	83	92
Number receiving 1 dose (1 cc.)	15	7	46

tion of antitoxin. Our group should be a more difficult one to immunize, because it is composed of a large percentage of persons who have been denied the primary immunizing stimulus, or who possess some defensive mechanism other than antitoxin which precludes their ever receiving this stimulus.

In our investigation (table 1) we have employed two doses of 1 cc. each at an interval of three weeks. A total of 104 subjects giving positive reactions to the Schick test were treated with toxoid, and the test was repeated from five to seven months after the last injection. Of this number, 89 received two doses and 15 received one dose. Of those receiving two doses, 83 or 92 per cent, were rendered negative; of those receiving one dose, 7, or 46 per cent, were rendered negative.

The differences in the results recorded in the literature as to the production of immunity are dependent on differences in the size and

11. Park, W. H.: Public Health and Hygiene, Philadelphia, Lea and Febiger, 1920.

12. Zingher, A.: Schick Test Performed on More Than 150,000 Children in Public and Parochial Schools in New York, Am. J. Dis. Child. **25**:392 (May) 1923.

13. Glenny, A. T.: J. Hyg. **24**:301, 1925.

number of the immunizing doses, as well as on the social and environmental status of the groups studied. Maloney and Fraser,[14] using two doses of 0.5 cc. each, were able to immunize 70 per cent of their subjects. Defries [15] immunized from 70 to 80 per cent with similar dosages. Zingher,[16] using three doses (0.5 cc., 0.5 cc. and 1 cc.), was able to obtain a 98 per cent immunization in his group. With two doses, he immunized 86 per cent and with one dose, 60 per cent of his subjects. Ramon and Helie,[1] in their review of the experience of the French workers, reported from 90 to 100 per cent immunization, most of their subjects receiving three doses. Martin and Loiseau [17] advised using 0.5 cc. for the third dose. In our own experience, we were able to obtain quite as satisfactory results with two doses of 1 cc. each (table 2).

As to the permanence of the immunization, it is too early to make any sweeping statement; however, reports in the literature tend to indi-

TABLE 2.—*Comparative Studies in Immunization with Toxoid*

	Number of Injections	Dosage, Cc.	Percentage Immunized
Maloney and Fraser	2	(1) 0.5 (2) 0.5	70
Defries	2	(1) 0.5 (2) 0.5	70-80
Zingher	3	(1) 0.5 (2) 0.5 (3) 1.0	90
Zingher	2	.....	86
Zingher	1	.....	60
Authors' series	2	(1) 1.0 (2) 1.0	92

cate a probable life-long immunity. Roubinowitch, Loiseau and Laffaille [18] tested patients at intervals of twelve, nineteen, twenty-three, twenty-four months and four years and found immunization to have persisted for these periods. Defries [15] suggested that the active immunity produced by diphtheria toxoid, by inference, should be of a character and duration like that which is naturally acquired by most persons by the time they have reached adult life.

REACTIONS FOLLOWING THE INJECTION OF DIPHTHERIA TOXOID

With the use of toxoid, as with that of toxin-antitoxin mixtures, there occur local and general reactions. The reports of various obser-

14. Maloney, P. G., and Fraser, C. J.: Am. J. Pub. Health **17**:1027, 1927.
15. Defries, R. D.: Pub. Health J. **19**:210, 1928.
16. Zinger, A.: Proc. Soc. Exper. Biol. & Med. **22**:462, 1925.
17. Martin, L., and Loiseau, G.: J. méd. franç. **15**:401, 1926.
18. Roubinovitch, J., Loiseau, G., and Lafaille, A., cited by Ramon (footnote 1).

vers [19] showed that there is a rather wide range in the incidence of reactions. These variations seem explicable on the basis of the fact that the observations were made on groups of diverse ages. The younger the age group, the smaller the incidence of reactions becomes. We, too, have noted that local reactions were rare and that general reactions never occurred in children under 7 to whom we administered toxoid.

The interpretation of what constitutes a reaction and its degree of severity depends, of course, on the individual concepts of each investigator. Without definite standards for evaluation of these reactions, there can be no exact concurrence in the various conclusions drawn. In our own study it was impossible to examine all reactions at the time of their occurrence. But, in so far as this series includes only nurses and medical students who were instructed what to watch for, their written or verbal reports, we think, can be accepted as accurate. Most of our subjects experienced some slight sensation of numbness or dis-

TABLE 3.—*Reactions to Toxoid*

Total number treated	205
Total number of reactions	51 (25%)

Grade	Reactions		Percentage of Total Number Treated
	Number	Per Cent	
Local (+)	3	5.8	1.5
Local (++)	12	23.5	5.8
Local (+++)	7	13.7	3.4
General	7	13.7	3.4
General and local	15	29.4	7.3
Ungraded	7	13.7	3.4

comfort at the site of the injection for a few hours. Only the twenty-four hour reactions were considered. Those with just pain or tenderness were graded as 1 plus L (local); those with moderate degree of swelling, and redness, as 2 plus L; those with marked swelling, redness, pain, tenderness and axillary adenitis as 3 plus L. The general reaction consisted of headache, nausea, anorexia, malaise and slight elevations of temperature. These were graded simply as G (general). Those with both general and local reactions were graded as G and L. In only one case was there a temperature of more than 100 (table 3).

An interesting observation was that in a few instances there was a reaction to the second injection when no reaction had followed the first, and vice versa.

19. Ramon and Helie (footnote 1). Zingher (footnote 16). Harvier, P., and Requin, J.: Paris méd. **59**:456, 1926. Park, W. H., and Schroder, M. C.: Comparative Merits of Old and New Preparations of Diphtheria Toxin-Antitoxin, J. A. M. A. **81**:1432 (Oct. 27) 1923. Maloney, P. G.: Am. J. Pub. Health **16**: 1208, 1925. Bloomberg, M., and Fleming, A. G.: Canad. M. A. J. **17**:801, 1927.

The reactions which followed the administration of toxin-antitoxin were accepted as being due to a tissue susceptibility to small amounts of toxin or to some degree of sensitivity to the horse serum present. Since neither of these elements is present in the toxoid solutions, a different explanation had to be sought.

There are present in the toxoid solution protein substances derived from the culture medium itself and from the products of autolysis and metabolism of the diphtheria bacilli. We believe that reactions following toxoid occur in certain persons who have been sensitized in some way to these specific proteins. This assertion is borne out by the fact that reactions are more frequent in patients convalescing from diphtheria,[1] that they rarely occur in young children, and that they are common in those persons who have a pseudoreaction to intradermal injections of the heated toxin.[20]

Of 20 of our adults with pseudoreactions to the Schick test, 15, or 75 per cent, had reactions to toxoid. However, a demonstrable sensitization to these proteins contained in toxoid is apparently not the only

TABLE 4.—*Relationship of Allergy and Reactions*

Number with positive allergic history	48
Number of reactors to toxoid	19 (40%)
Number with negative allergic history	64
Number of reactors to toxoid	10 (16 %)
Number with positive allergic history and pseudoreactions to Schick test	10
Number of reactors to toxoid	9 (90%)

cause for these reactors, as these figures might suggest, for of a total group of 51 reactors to toxoid, only 15, or 29 per cent, had pseudoreactions to the Schick test.

We suspected that reactions to toxoid would occur mainly, if not entirely, in persons with an allergic background. With the hope of throwing some additional light on the problem of reactions, we made an attempt to determine, by obtaining individual histories, whether allergy bears some intimate relationship to the occurrence of those reactions. We are aware, of course, that an investigation by means of questionnaires may be fraught with inaccuracies (table 4).

In a group of 112 adults, we found that there were 48 with either a definite family or personal history of one of the allergic diseases. Of this group of 48, 19, or 40 per cent, were reactors. The incidence is not large, and yet we consider it significant when this is compared with the larger group of 64 adults with negative histories, in which group there were only 10, or 16 per cent, reactors.

20. Park (footnote 11). Defries (footnote 15). Zingher (footnote 16). Roubinowitch, J.; Loiseau, G., and Lafaille, A.: Bull. et mém. Soc. méd. d. hôp. de Paris **48**:782, 1924.

An even more convincing proof of the part that sensitization must play in the production of these reactions is the fact that of 10 persons with both a positive allergic history and a pseudoreaction to the Schick test, 9, or 90 per cent, had reactions after administration of toxoid.

The fact that reactors to toxoid are more readily immunized than nonreactors [21] is but another point in favor of the allergic theory as an explanation of these reactions, for it may be that the subinfective doses of diphtheria with which people come in contact produce a sensitization to the specific protein of the Klebs-Loeffler bacillus, and likewise induce a partial immunity to the toxin. Our observations in this regard, though based on a small group of cases, we believe are significant (table 5).

It is interesting that, of the group composed of reactors to toxoid, none gave a true positive reaction to the Schick test after the one injection of toxoid. Those that did not become negative to the test

TABLE 5

Number receiving one dose of toxoid		15
Number rendered negative to Schick test		7
Reactors to toxoid	4	
Nonreactors to toxoid	3	
Number of reactors to toxoid receiving one dose		7
Rendered negative to Schick test	4	
Rendered pseudoreactive to Schick test	3	
Remaining positive to Schick test	0	
Number of nonreactors to toxoid		8
Rendered negative to Schick test	3	
Remaining positive to Schick test	5	
Rendered pseudoreactive to Schick test	0	

developed pseudoreactions to it. Although determinations of antitoxin content were not made on the blood of these persons, it is not at all unlikely that the three with pseudoreactions were actually immunized.[9] While these were probably of the fundamentally sensitized group, as evidenced by the fact that they were reactors to toxoid, they did not manifest a skin sensitization to the protein contained in the heated toxin of the original control test. Roubinovitch and his associates [22] have also noted that in the sensitized group a single administration of toxoid is a sufficient stimulus to induce a specific skin sensitization to the protein of the toxin solution (heated or unheated). Why four of our reactors to toxoid became negative to the Schick test instead of developing pseudoreactions is difficult to explain.

In the past, when toxin-antitoxin was employed by us as an immunizing agent we kept no records as to the incidence of local or general reactions that followed. Hence, we can offer no comparative

21. Zingher (footnote 16). Bloomberg and Fleming (footnote 19, sixth reference).

22. Roubinowitch et al. (footnote 20, fourth reference).

statistics of our own. However, Park and Schroder,[23] also reporting observations on adults, showed that in their series of 117 persons treated with the 0.1 L plus toxin-antitoxin, there were reactions in 74 per cent. When the toxoid was employed in our larger series, 25 per cent of the patients had reactions. Park and Schroder did not record general reactions, while several (11 per cent) occurred in our series. Too great emphasis cannot be placed on this comparison, for, as we have pointed out before, our standards of determining what constitutes a reaction may be different from those of other observers.

While the various toxin-antitoxin mixtures have served as efficient immunizing agents, as is shown by the marked reduction in the incidence of diphtheria in this country following their employment on a broad scale, nevertheless, experience with toxoid in the last few years would tend to indicate that in its use certain important advantages have

TABLE 6.—*Comparative Studies of Immunity Production Secured with Toxoid and Toxin-Antitoxin*

Observer	Subjects	Material	Dosage	Percentage of Immunity
Zingher	Children	Toxin-antitoxin	0.1 L+ 3 doses	91
Zingher	Children	Toxoid	0.5 cc. 0.5 cc. 1.0 cc.	98
Park and Schroder	Adults	Toxin-antitoxin	3.0 L+	87
Park and Schroder	Adults	Toxin-antitoxin	0.1 L+	83
Authors' series	Adults	Toxoid	1.0 cc. 1.0 cc.	92

been demonstrated. Furthermore, certain objections which had been advanced against toxin-antitoxin do not obtain in the case of toxoid (table 6).

In testing the relative antigenic properties of toxin-antitoxin and toxoid, Zingher [16] administered toxin-antitoxin to half the children in 3 large metropolitan schools and toxoid to the other half. With 3 doses of toxoid (0.5 cc., 0.5 cc. and 1 cc.), he successfully immunized 98 per cent, and with 3 injections of the 0.1 L plus toxin-antitoxin 91 per cent were rendered immune.

In adults, Park and Schroder [23] immunized 87 per cent with the 3 L plus toxin-antitoxin and 83 per cent with the 0.1 L plus. Zoeller [24] immunized 100 per cent of his 47 adults. Of our eighty-nine adults who received two doses of toxin, 92 per cent were rendered negative to the Schick test.

23. Park and Schroder (footnote 19, fourth reference).

24. Zoeller, C., cited by Ramon (footnote 1).

Our experience with toxin-antitoxin has been none too satisfactory. The experience of Rhoads [25] with the nurses of Cook County Hospital is not unlike our own. He found that within three years and not less than three months after 3 injections of toxin-antitoxin, 67 per cent of 64 nurses still showed positive reactions. We retested 75 nurses who had received 3 doses of toxin-antitoxin at a minimum period of one year and a maximum of three years before the retest. Only 41, or 55 per cent, were rendered negative. Another significant fact is that in a period of twenty-six months, 10 of our student nurses developed definite pharyngeal diphtheria in spite of the fact that they had received toxin-antitoxin not less than one year or more than three years before the development of the diphtheria.

Evidence has been presented both in favor of and against the theory that the horse serum content of toxin-antitoxin may induce a sensitization to subsequent injections of horse serum. In reviewing a series of patients who had received scarlet fever or diphtheria antitoxin, Spicer [26] noted no appreciable difference in the incidence of serum reactions in the group that had previously received toxin-antitoxin than in the group that had not. Bauer and Wilmer [27] arrived at essentially the same conclusion. Furthermore, they noted no ill effects when toxin-antitoxin was administered to asthmatic patients.

On the other hand, the clinical experience of Park,[28] Waldbott [29] and Stewart [30] would tend to refute the idea that toxin-antitoxin is incapable of sensitizing persons to horse serum. Waldbott reported eight cases of asthma precipitated by administration of toxin-antitoxin. Park noted an incidence of serum sensitivity in from 72 to 75 per cent of those children who had received toxin-antitoxin as compared to an incidence of 50 per cent in those children who had not.

As early as 1914, Cowie [31] pointed out that anaphylactic shock is more likely to follow reinjection after a small sensitizing injection of horse serum (from 0.1 to 0.00001 cc.) than after large ones (10, 20

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25. Rhoads, P.: Commercial Preparations of Diphtheria Toxin-Antitoxin, J. A. M. A. **90**:254 (Jan. 28) 1928.

26. Spicer, S.: Effect of Previous Administration of Antitoxin and Toxin-Antitoxin of Serum Reactions, J. A. M. A. **90**:1778 (June 2) 1928.

27. Bauer, E. L., and Wilmer, H. B.: Toxin-Antitoxin; Hypersensitivity to Its Protein Content, J. A. M. A. **86**:942 (March 27) 1926.

28. Park, W. H.: J. Immunol. **9**:17, 1924.

29. Waldbott, G.: Diphtheria Prophylaxis Among Asthmatic Patients, J. A. M. A. **90**:290 (Jan. 28) 1928.

30. Stewart, C. A.: Anaphylactic Reactions Following Administration of Serum to Children Previously Immunized Against Diphtheria, J. A. M. A. **86**: 113 (Jan. 9) 1926.

31. Cowie, D. M.: Studies on the Incubation Period: I. Serum Disease, Am. J. Dis. Child. **7**:253 (April) 1914.

or 30 cc.). Hooker [32] showed that even with the 0.1 L plus mixtures of toxin-antitoxin which contain only 0.00014 cc. of globulin he was able to procure hypersensitiveness in a noteworthy proportion of human subjects.

Twelve of our student nurses, 10 of whom we have already referred to, within a recent twenty-six month period contracted diphtheria. Ten of these had received toxin-antitoxin a year previously, and the remaining 2 received toxin-antitoxin one month before. None of these gave a history of ever having received any other form of horse serum. During this same twenty-six month period, 7 students from the university were admitted to our contagious ward with diphtheria. Of these, none gave a history of ever having received toxin-antitoxin or horse serum. Ten of the nurses were treated with the usual therapeutic doses of diphtheria antitoxin. Six, or 60 per cent, had definite serum reactions, 1 immediate and 5 delayed. Six of the students from the university were treated, and only 1, or 16 per cent, had evidence of serum sickness.

Although we have never met with accidents following the use of toxin-antitoxin, we do feel that the subsequent sensitization which it induces to horse serum is a serious and valid objection to its use, particularly when another and a superior antigen which contains no horse serum is available.

SUMMARY

1. Experiences with toxoid in the active immunization against diphtheria are recorded; the favorable results obtained confirm those previously reported by other observers. In a well controlled group of 104 adults with positive reactions to the Schick test, it was found that in 83 (92 per cent) of 89 who were treated with two doses (1 cc. each) of toxoid the reaction became negative. Of 15 persons receiving one dose (1 cc.) of toxoid, the Schick reaction was likewise rendered negative in 7 (46 per cent).

2. In the routine employment of the Schick test, certain sources of error and the possibilities of misinterpretation arising therefrom were pointed out.

3. The majority of the subjects comprising our series came from rural districts. A high incidence of positive reactions to the Schick test (73 per cent) was found in this group, and this high incidence stands in interesting contrast to the low proportion of persons susceptible to diphtheria found in well populated areas.

4. The interesting phenomenon of reactions to the administration of toxoid was studied. While in a general way it was found that local reactions to toxoid are much less frequent as compared with those

32. Hooker, S. B.: J. Immunol. **9**:7, 1924.

following toxin-antitoxin, general reactions to toxoid were observed with greater frequency. It was noted that both general and local reactions to toxoid were rare in young children.

5. Studies on the nature of these reactions to toxoid tend to indicate that allergy plays an important rôle in their manifestation. Particularly striking was the high incidence of reactions to toxoid in persons presenting both a history of allergy and a pseudoreaction to the Schick test.

6. Certain important advantages in the use of toxoid in lieu of toxin-antitoxin, both on the basis of personal experience and on evidence from the literature, were enumerated. The use of toxin-antitoxin entails the possibility of the production of a sensitization to horse serum, whereas with the employment of toxoid such a possibility is obviated. Our own past experience with toxin-antitoxin indicates that as an immunizing agent it is inferior to toxoid. The relatively greater stability, innocuousness and need for fewer injections of toxoid were additional advantages mentioned.

CONCLUSIONS

The toxoid solution is an immunizing agent the antigenic properties of which are of unquestionable value. We believe, from our own experience and that of others, that the assertion is warranted that toxoid merits the preference in the choice of an immunizing agent in the prophylaxis of diphtheria.

DIRECT LARYNGOSCOPY AS A METHOD FOR CULTURAL STUDIES OF PULMONARY SECRETIONS IN INFANTS AND IN CHILDREN *

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Because infants and children fail to expectorate or have a tendency to swallow their coughed up secretions and sputums, various indirect methods have been employed for the purpose of obtaining material for cultural studies. These have varied from that of tickling the pharynx and having the patient cough into Petri dishes containing culture mediums, to that of introducing an aspirating needle directly through the wall of the chest to obtain material for study.

Direct laryngoscopy affords a simple method for procuring secretions from the larynx, trachea or bronchi of infants and children. It is done quickly, does not provoke much resistance from the patients and exerts no harmful influence on their general condition. No anesthesia is used. The instruments needed are a direct laryngoscope, a suction apparatus, a Yankauer suction tube and a specimen collector. If smears are to be made, applicators or swabs are necessary. The procedure may be performed either in the bed of the patient or on the table. If the child is not too ill to be moved, the table is preferable. The larynx is exposed with the laryngoscope. The suction tip, which has been connected to the specimen collector, is then introduced into the larynx, and if secretion is present this is aspirated. Usually the child will cough, and enough material will be available for the purpose needed. The suction tip may be introduced farther down the pulmonary tree, according to the desire of the operator. The suction tube is then withdrawn. One must be careful at this stage to avoid aspirating the pharyngeal secretions which may be present. This is assured by removing the vacuum pressure from the suction tip as it is withdrawn from the larynx. The tip of the suction tube is then put into a test tube of ordinary sterile bouillon, and a small quantity of the matter is aspirated in order that any secretion which may be lying within the lumen of the suction tube may be gathered into the specimen collector.

Enough material is obtained in this manner for cultural study. The secretion will usually collect as a supernatant layer in the tube. If studies of the various organisms are desired, a platinum loop may be inserted into the tube and different mediums may be inoculated imme-

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* From the Pediatric and Laryngological Services of the Mount Sinai Hospital, New York.

diately. If pneumococcus typings are desired, this fluid can be injected into the peritoneum of a mouse according to the routine way. Sometimes the material which has been aspirated is so thick that it may be necessary to grind up the bouillon mixture with sand. I have been using this method of obtaining secretions in infants and children for the typing of pneumonias, thus determining the therapy by specific serums.

In a similar manner, direct laryngoscopy may be utilized for the purpose of making smears. Metal applicators with sterile absorbent cotton or long swabs may be introduced into the larynx or trachea and smears made. This is especially desirable in cases in which tuberculosis or diphtheria is suspected. Blood plates may be streaked or other mediums may be inoculated, using applicators, but I have found the aspiration method the preferable one because of its rapidity and the absence of contamination.

The laryngeal pictures of bronchopneumonias and lobar pneumonias are those of congestion and are more marked in the bronchopneumonic forms. These observations may be used as diagnostic adjuvants in cases in which the diagnosis is not clear, as in cases of abdominal pains, tenderness and doubtful chest signs, and a differential diagnosis rests between that of a pulmonary condition and an intra-abdominal disease. Laryngoscopies in cases of streptococcic peritonitis and appendicitis have revealed normal larynxes. It is therefore suggested that when the differential diagnosis lies between pneumonia and other conditions, laryngoscopy be utilized as a clinical aid. In a recent case of questionable pneumonia in an infant aged 14 months laryngoscopy was performed for the purpose of obtaining material for culture. It was noted that the larynx was normal. It was ascertained that this infant had had periods of fever, cough and signs simulating asthma without definite chest findings of pneumonia. Eventually, the condition proved to be one of allergy. The significance of a normal larynx in this case excluded the diagnosis of an acute process of the lung.

SUMMARY

1. Direct laryngoscopy is a simple method for obtaining secretion from the larynx, trachea or bronchi of infants and children.
2. Aspirated secretions may be studied bacteriologically.
3. Smears may be made and studied, e.g., tuberculosis, diphtheria.
4. Pneumonias in children may be classified in this way.
5. Laryngeal pictures of pneumonias may be utilized as aids in differential diagnosis.

Results obtained with this method will be published in a subsequent paper in which especial attention will be given to the bacteriology and typing of micro-organisms in cases of pneumonia occurring in infants and children.

OTITIS MEDIA IN INFANCY

ITS DIAGNOSIS BY MEANS OF CULTURES TAKEN FROM THE MIDDLE EAR DESCRIPTION OF METHOD *

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Otitis media is one of the most frequent diseases of childhood. On account of the size of the aural canal and the tympanic membrane, it is difficult to obtain sterile cultures from the middle ear.

A method will be described whereby pus can be aspirated from the middle ear, and the organism can be cultured and isolated; it has proved satisfactory, and we believe that it can be easily carried out.

This study was made on children from 2 months to 2 years of age, selected indiscriminately, when the clinical evidence of otitis media was present.

TECHNIC

The contents of the middle ear are obtained by means of a specially made needle, 19 gage, 3½ inches (8.9 cm.) long. To the needle, a glass observation tube (glass window) is added. A piece of soft rubber tubing, 3 inches (7.6 cm.) long is placed between the observation tube and a glass mouth piece as shown in the figure. With this apparatus, the contents of the middle ear can be withdrawn by aspiration. Before the apparatus is used, it is sterilized by autoclaving in a test tube with a cotton stopper.

Apparatus used in aspirating contents of middle ear.

The child is wrapped in a blanket and placed on an examining table. The head is held quiet by an assistant. The cerumen and the contents of the aural canal are carefully removed. Absolute alcohol is then dropped into the canal. Next, sterile cotton is inserted and removed after five minutes. A sterile speculum attached to an electric auriscope is placed in the canal. The needle is inserted into the speculum and through the drum. By suction with the mouth, the contents of the middle ear are withdrawn into the observation tube. The material obtained is immediately transferred into 1 cc. of sterile physiologic sodium chloride solution in a small test tube.

Cultures are made from the suspension in physiologic sodium chloride solution. The material is placed in each of two tubes of veal infusion pneumococcus broth, *p*H 7.4. In addition, streaks are made with a platinum wire on a beef extract, agar

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blood plate, p_H 7.8. At the same time, a smear of the suspension is made, and examined with Gram's stain.

Observations are made before the needle is inserted as to the appearance of the drum, its color and the amount and position of the bulging. This is done in order to ascertain whether the organism cultured from the contents of the middle ear is associated with any characteristic changes in the tympanic membrane.

Summary of Observations on Forty-Three Middle Ears

Case	Temperature, F.	Diagnosis	Age	Middle Ear	Smear Examination	Organism Cultured
1	100.8	Tetany; otitis media.....	6 mo.	R.	Leukocytes, bacilli	B. coli communis
2	100.6	Otitis media.....	14 mo.	R.	Leukocytes, cocci	Staphylococcus aureus
3	104.0	Tonsillitis; otitis media....	6 mo.	L.	Leukocytes, cocci	Staphylococcus aureus
4	100.0	Malnutrition; otitis media.	8 mo.	R.	Leukocytes, cocci	Staphylococcus aureus
5	100.8	Otitis media.....	7 mo.	R.	Leukocytes, cocci	Staphylococcus aureus
6	100.0	Otitis media.....	9 mo.	R.	Leukocytes, cocci	Staphylococcus albus
7	101.0	Pneumonia; otitis media...	17 mo.	L. & R.	Leukocytes, bacilli	B. coli communis
8	100.0	Otitis media.....	8 mo.	L.	Leukocytes, cocci	Staphylococcus albus
9	100.0	Otitis media.....	8 mo.	L. & R.	Leukocytes, cocci	Staphylococcus aureus
10	101.2	Otitis media.....	9 mo.	L.	Leukocytes, cocci	Staphylococcus aureus
11	100.0	Otitis media.....	6 mo.	L.	Leukocytes, cocci	Staphylococcus aureus
12	101.0	Otitis media.....	7 mo.	R.	Leukocytes, bacilli	B. coli communis
13	103.0	Otitis media.....	6 mo.	R.	Leukocytes, cocci	Hemolytic streptococci
14	100.0	Otitis media.....	6 mo.	R.	Leukocytes, cocci	Staphylococcus aureus
15	101.8	Otitis media.....	7 mo.	L.	Leukocytes, cocci	Staphylococcus aureus
16	103.2	Otitis media.....	5 mo.	L. & R.	Leukocytes, cocci	Staphylococcus aureus
17	104.6	Pyelitis; otitis media.....	8 mo.	L. & R.	Leukocytes, cocci	Staphylococcus aureus
18	102.0	Pneumonia; otitis media...	6 mo.	R.	Leukocytes, cocci	Staphylococcus aureus
19	102.0	Pharyngitis; otitis media..	16 mo.	R.	Leukocytes, cocci	Staphylococcus aureus
20	103.0	Otitis media.....	8 mo.	L.	Leukocytes, bacilli	B. coli communis
21	103.0	Pneumonia; otitis media...	3 yr.	R.	Leukocytes, cocci	Hemolytic streptococci
22	102.4	Pneumonia; otitis media...	2 yr.	L.	Leukocytes, cocci	Hemolytic streptococci
23	103.6	Pneumonia; otitis media...	7 mo.	L.	Leukocytes, bacilli	B. coli communis
24	103.0	Otitis media.....	2 mo.	L. & R.	Leukocytes, cocci	Staphylococcus aureus
25	101.0	Otitis media.....	7 mo.	L. & R.	Leukocytes, cocci	Staphylococcus aureus
26	100.0	Rickets; otitis media.....	6 mo.	L. & R.	Leukocytes, cocci	Staphylococcus albus
27	100.0	Pneumonia; otitis media...	10 mo.	L. & R.	Leukocytes, cocci	Staphylococcus albus
28	102.0	Tonsillitis; otitis media....	7 mo.	R.	Leukocytes, bacilli	B. coli communis
29	100.0	Otitis media.....	3 mo.	L. & R.	Leukocytes, cocci	Staphylococcus aureus
30	102.4	Otitis media.....	6 mo.	L.	Leukocytes, cocci	Staphylococcus aureus
31	102.0	Pneumonia; otitis media...	7 mo.	L.	Leukocytes, cocci	Staphylococcus albus
32	100.0	Pneumonia; otitis media...	5 mo.	L. & R.	Leukocytes, cocci	Staphylococcus albus
33	101.0	Pharyngitis; otitis media..	6 mo.	L.	Leukocytes, bacilli	B. coli communis

RESULTS

Thirty-three children were studied, and cultures were made by this method from a total of forty-three middle ears. In some of the children, both ears were examined.

The organisms obtained were *Staphylococcus aureus,* twenty-four cultures; *Staphylococcus albus,* eight; hemolytic streptococcus, three, and the colon bacillus, eight. We considered these organisms the predominating organism only when we were able to isolate and identify the same organism from each of the broth tubes and the agar blood plate. In the children in whom cultures were made from both middle ears, the same organism was isolated from each middle ear.

A question arises whether the staphylococcus group was overgrowing the other organisms present in the middle ear. A suspension of equal amounts of staphylococci, pneumococci and hemolytic streptococci was made. A portion of the suspension was then cultured in the same broth mediums and streaked on the agar blood plates, the same medium used in this study. All organisms could be grown and could be isolated and identified. From this experiment we felt that the staphylococcus group was not overgrowing other organisms in the middle ear, and that the medium was suitable for culturing the most prominent organisms found in otitis media.

A comparison of the description of the drum and the type of organism obtained shows nothing significant. In the staphylococcus and colon group the drum was dull gray; bulging occurred in all quadrants, and the pus was thick and tenacious. In the hemolytic streptococcus group, only three cases were obtained: the tympanic membrane was vivid red; the bulging was less marked, and the pus obtained was thin and serous.

The smears contained leukocytes in the various stages of degeneration. When staphylococci or streptococci were the predominating organisms, they were found as gram-negative cocci scattered throughout the smear. When the colon bacilli were the predominating organisms, they were found throughout the smear as gram-negative rods.

SUMMARY AND CONCLUSIONS

A satisfactory method for obtaining sterile cultures from the middle ear is described.

The medium used is satisfactory for growing the common organisms found in otitis media.

By a comparison of the smears and cultures, a true diagnosis of otitis media can be made.

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BERIBERI IN INFANTS*

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I do not pretend to cover the subject of beriberi in this paper, but I have written it chiefly to report several cases which appear to correspond to the usual picture of that disease in infants. The four cases considered have been seen in the space of the past six months, and it appears that similar cases have been previously noted by physicians in Charleston, but have never been recorded as cases of beriberi. Vedder,[1] an authority on the subject, stated that "no case of an infant affected by this disease has ever been reported" in the United States. The literature seems to contain no reference to local cases, and a recent article by Hoobler[2] reiterates that beriberi does not appear in infants in this country. The only reference to beriberi in children in the United States is found in an article by Scott and Hermann,[3] who stated that in Louisiana "children are also known to have acquired the disease," but these writers make no amplifying statement.

If the diagnosis of infantile beriberi is to be applied only to nursing infants of mothers with beriberi, then the cases reported in this paper may perhaps belong in some other category, though the symptoms presented appear to be the same as those described by writers familiar with the disease as it occurs in infants in Japan and elsewhere.

Hoobler[2] has described symptoms which he attributes to a partial deficiency of vitamin B in the diet of infants. Some of the symptoms are gastro-intestinal disturbances, restlessness, weakness, feeble cry, pallor, oliguria, anorexia and sluggish knee reflexes. The fully developed picture of oriental beriberi resulting from a practically complete absence of vitamin B is characterized by edema, aphonia, peripheral neuritis and cardiac hypertrophy. Concerning the heart it is said that there is an accentuation of the pulmonic sound, usually an absence of murmurs, but a marked hypertrophy, particularly of the right side. The

* Submitted for publication, Feb. 25, 1929.

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1. Vedder, Edward B.: Beri-beri, in Abt: Pediatrics, Philadelphia, W. B. Saunders Company, 1926, vol. 2, chap. 27, p. 815.

2. Hoobler, B. R.: Symptomatology of Vitamin B Deficiency in Infants, J. A. M. A. **91**:307 (Aug. 4) 1928.

3. Scott, Leonard C., and Hermann, George E.: Beri-beri (Maladie des Jambes) in Louisiana, J. A. M. A. **90**:2083 (June 30) 1928.

apparent hypertrophy of the heart has been attributed [4] to retention of fluid in the cardiac tissues, and there is usually no considerable abnormality in the electrocardiagraphic picture.

As I believe that the following cases conform fairly well to the description of beriberi, I have ventured to report them as such. The first patient was not treated, while the other three responded well to a diet rich in vitamin B.

REPORT OF CASES

CASE 1.—A colored infant was first seen at a health center when she was 5 weeks old. Having been adopted under vague circumstances, she had apparently never been breast-fed, and was said to be on half strength dried milk and sugar mixture, 4 ounces every three hours. She showed at this time poor nutrition, weighed 7 pounds and 9 ounces (3,430.2 Gm.) and had a papular and crusted rash over the whole body. No cardiac abnormalities were present.

A week later, after a change in the formula and treatment with a sulphur ointment, she appeared much better, showed an improvement in the condition of the skin, and had gained 12 ounces (340 Gm.). She was constipated. After another week she was readmitted with the history of refusal of food, vomiting and loose stools for several days. She had lost 9 ounces (255 Gm.). The temperature by rectum was 100 F., and a marked pallor was present.

The child was referred to the hospital where no additional physical observations were recorded. There was neither edema nor cardiac abnormality. The vomiting did not continue and the diarrhea appeared to be mild. The infant took a formula of lactic acid milk (dried) and dextrimaltose very well, and began to gain slightly. The rectal temperature never exceeded 100 F., and usually was about 97 F. Orange juice was given regularly.

For three weeks there were no remarkable developments. Then a slight generalized edema began to appear and gradually increased. The pulse became rapid, but no cardiac murmur was heard. A week later a systolic murmur was detected over the heart, especially on the right of the sternum; there was an increase in the area of cardiac dulness, and a few râles and high-pitched breath sounds appeared in the lower lobe of the right lung. Roentgen examination showed a "heart so large that no lung detail can be made out," and films of the extremities were negative. The child lay almost motionless.

For the next five days there was an increase in the edema. The knee reflexes disappeared, and the liver was found to be about 5 cm. below the costal margin. The patient died at the age of 13 weeks, after being in the hospital six weeks.

Laboratory examinations were negative throughout. The stool showed no ova; the urine was clear on two examinations after the appearance of the edema; the Wassermann and Kahn tests were negative. The hemoglobin content was 80 per cent (Dare) on two examinations. The blood count on admission was: white blood cells, 5,240; lymphocytes, 44.5 per cent; polymorphonuclears, 54 per cent; large mononuclears, 1.5 per cent; eosinophils, 0. One month later, the blood count showed: white blood cells, 6,680; lymphocytes, 41 per cent; polymorphonuclears, 58 per cent; large mononuclears, 0, and eosinophils, 1 per cent.

The diet was varied between protein milk (dried) and mixtures of lactic acid milk (dried) with dextrimaltose. Orange juice was given daily. A digitalis preparation seemed to have no appreciable effect on the heart.

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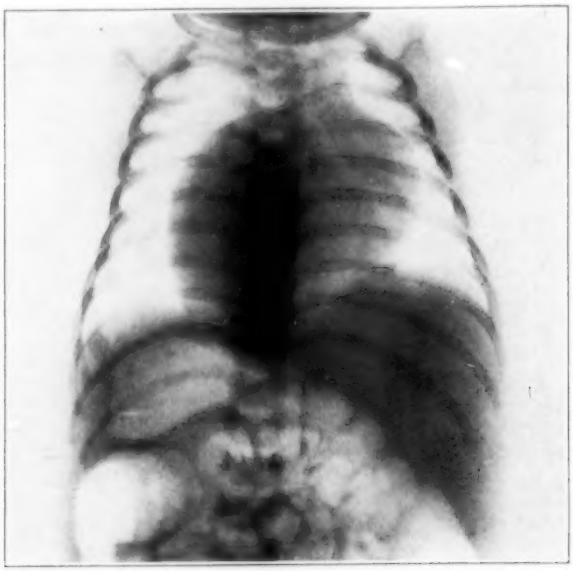
4. Wenckeback, K. F.: Heart and Circulation in a Tropical Avitaminosis (Beri-beri), Lancet **215**:265 (Aug. 11) 1928.

Here, then, was a child who had supposedly been fed on a fairly reasonable milk and sugar mixture, but who failed to gain, developed diarrhea and edema without evident cardiac or renal abnormality, then showed a rapid pulse and cardiac hypertrophy, with loss of knee reflexes, and a final phase of hepatic enlargement and cardiac failure. This would seem to be sufficient evidence for making a diagnosis of infantile beriberi.

CASE 2.—An infant, colored, aged 2½ months, was brought to an outpatient department with the complaint of a cold, cough and constipation. She was an only child (only pregnancy) and was breast-fed at night, and fed on a half strength dried milk mixture (a total of only 8 ounces) while the mother was working during the day. Her nutrition was very poor, and her weight only 8 pounds and 5 ounces (3,770.4 Gm.). Neosilvol was prescribed for the rhinitis present, and the mother was urged to nurse the baby more often.



Cardiac hypertrophy in infantile beriberi

Two weeks later, the patient was seen again and was still constipated and not much improved. She was given a new formula, and five weeks later was back with a "cold." About two months after this, when she was about 6½ months old, she was brought in with the complaint of "cold and fever." She showed poor nutrition, weighing 8 pounds and 2 ounces (3,685.4 Gm.), and had edema of the face, legs and thighs; knee reflexes were absent. It appeared that since the age of about 2½ months she had been getting nothing but an uncertain dried milk mixture.

Results of the Wassermann and Kahn tests and tests of the urine were negative. The hemoglobin content was 55 per cent (Dare). The blood count was: leukocytes, 9,550; lymphocytes, 52 per cent; polymorphonuclears, 45 per cent; large mononuclears, 1 per cent, and eosinophils, 2 per cent.

The infant was put on a formula of lactic acid milk and dextrimaltose, with orange juice, cod liver oil and one and a half tablets of brewers' yeast daily.

The temperature ranged between 98 and 100 F. by rectum. In a week the edema was gone, and two weeks after admission the weight had increased 6 ounces (170 Gm.). The knee reflexes returned. The infant was discharged to the parents.

About three months after leaving the hospital, the infant was brought back to the outpatient department presenting a typical emaciated, marasmic appearance and a large abscess of the subcutaneous tissue of the neck. There had been no return of the edema, although the diet had apparently consisted of a vague dried milk formula, cream of wheat and orange juice given spasmodically.

The history of improper feeding, the edema, the absence of knee reflexes, and the negative urinary and other observations, all gave the impression that the patient was suffering from a dietary deficiency; the rapid response to the use of a varied diet, rich in vitamin B, seemed to justify a diagnosis of beriberi, even though the picture was not completed.

CASE 3.—A colored boy, aged 1 year, second child of his parents, had been born at full term. He had been breast-fed for eleven months. For four weeks, he had had "fever, weakness" and occasional diarrhea. For about two weeks, he had had some swelling of the feet and puffiness of the face. A month before he had been weaned because his mother developed "rheumatism" (beriberi in mild form?) and since that time he had eaten nothing but hominy.

He weighed 16 pounds and 3 ounces (7,342.4 Gm.), and presented fair nutrition, and edema of the face and extremities; the knee reflex was absent on the right and sluggish on the left. The stool was normal on two examinations; the urine showed an occasional white cell only; the hemoglobin content was 80 per cent (Dare) and the red cells 4,840,000. Leukocytes were 17,960, with lymphocytes 11 per cent, polymorphonuclears, 88 per cent, and transitionals 1 per cent. The x-ray picture of the heart was negative.

At the end of a week on a diet of milk, cereal, soup and apple sauce, reinforced by three tablets of brewers' yeast daily, the edema had disappeared, and the knee reflexes were active. The temperature ranged from 98 to 100 F. by rectum. At the end of seventeen days there was a total loss of 4 ounces in weight, but marked improvement in the general condition of the child, so that he was discharged from the hospital.

Five weeks later he was back again, having been edematous for three weeks, and having subsisted on a diet of hominy and dregs of breast milk. This time, besides the edema, there was an inconstant cardiac arrhythmia, a palpable spleen and fairly active knee reflexes. The hemoglobin content was 90 per cent (Dare). The blood count showed: white blood cells, 9,850; lymphocytes, 33 per cent; polymorphonuclears, 66 per cent, and basophils, 1 per cent. The Wassermann and Kahn tests were negative.

The child appeared to be in pain when he was handled. The temperature ranged from 97 to 100 F. At the end of sixteen days, under the same diet previously used, the heart was normal, the edema had disappeared and the child could stand well. In a month he had gained 3 pounds (1,360 Gm.) and was discharged in good general condition.

This case presents several features similar to those in the second case. A diet of hominy, with a background of breast milk alone up to the age of 11 months, poor nutrition, edema, absent or sluggish knee reflexes, the response to diet, the return of symptoms when the proper diet was omitted and the second period of improvement when it was instituted again, all together lead to the diagnosis of beriberi.

CASE 4.—A colored boy, aged 8 months, had a negative past history. He had been breast-fed for seven months, and was then given condensed milk and sugar. His mother complained that he had "fever and straining," and she was advised to put him on a proper diet.

A week later, there was not much change. An apical systolic murmur was noted. Two weeks later, he was seen again, and it was found that he had still been getting condensed milk. Then he disappeared from observation for three months, to return with the complaint of swelling for the previous week. The mother confessed that the infant had had only variable amounts of a dried milk mixture, sugar, cream of wheat and corn meal since the last visit. He was then about 1 year old, emaciated, anemic and had edema of the legs and active knee reflexes. Parietal bosses were present; he had four teeth, and showed a precordial systolic murmur of soft quality. His weight was 12 pounds and 10 ounces (5,726.6 Gm.).

The urine showed a trace of albumin. The hemoglobin content was 40 per cent (Tallqvist). The blood count showed: white blood cells, 12,730; lymphocytes, 62 per cent; polymorphonuclears, 33 per cent; large mononuclears, 3 per cent; eosinophils, 1 per cent; basophils, 1 per cent. An x-ray picture of the heart was negative. The Wassermann and Kahn tests were negative.

He improved rapidly on a diet of dried milk mixture, cereal, extract of malt and cod liver oil, orange juice, and yeast tablets three times daily. The edema disappeared in a week, and in twelve days he gained 1 pound and 9 ounces (708.7 Gm.). The urine at that time still showed a trace of albumin.

This case was less definite in its manifestations, but probably belongs in the same class as the others.

COMMENT

It was felt that the last three patients were treated in time to prevent the development of the full symptomatology of beriberi, but nevertheless the condition might well be diagnosed as such.

It is more than probable that cases such as these not infrequently occur in this section, particularly among the negroes, whose ideas of feeding infants are usually vague and inadequate. Hoobler has suggested that many rather indefinite symptoms may result from a partial deficiency of vitamin B, which is not ordinarily supplied as a routine to young infants, and no doubt the picture may often go on to completion in the form of well developed beriberi. Since two of the cases described were at first thought to be nephritic on account of the edema, and since the first case was recognized only in retrospect, it has seemed appropriate to call attention to the fact that this type of nutritional disturbance has occurred recently in Charleston, and to assume that it is of fairly frequent occurrence in other places where similar conditions exist.

ICTERUS NEONATORUM *

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In discussing icterus neonatorum, it is of great importance to have a clear idea of the definition of icterus in general. The old definition of icterus as a symptom characterized by coloration of the skin, mucous membranes, and fluids of the body by bile pigment requires revision. Since van den Bergh [1] introduced the Ehrlich diazo reaction as a test for minute quantities of bilirubin in the blood serum, it is known that icterus may be present without any discoloration of the skin (icterus sine ictero). We stress this point because in the literature on icterus neonatorum the distinction between icteric and nonicteric infants is often made. This division, however, can no longer be made, for it has been shown that every child has icterus at birth, whether the condition is visible or not. Thus, Cserna and Liebman,[2] Zamorani,[3] Knoepfelmacher and Kohn [4] found that the umbilical cord blood gave an indirect van den Bergh reaction in all cases. We may, therefore, define icterus in general as an increase of bile pigment in the blood serum, which, if great enough, may cause a yellowish discoloration of skin, mucous membranes and fluids of the body.

TYPES OF ICTERUS IN THE NEW-BORN INFANT

Before entering into the details of icterus neonatorum, it is important to point out the types of jaundice which one may find in the new-born infant. McNee [5] classified jaundice into three types: (1) obstructive

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* This research had been made possible by a grant from the James Cooper Fund.

1. Van den Bergh: Der Gallenfarbstoff im Blute, Leyden, 1918; Presse méd. **29**:441, 1921. Van den Bergh and Mueller, in Abderhalden: Handbuch der Biologie Arbeitsmethoden, pt. 4. Van den Bergh and Snapper: Deutsches Arch. f. klin. Med. **110**:540, 1913; Berl. klin. Wchnschr. **51**:1109, 1914; **52**:1081, 1915.

2. Cserna and Liebman: Klin. Wchnschr. **2**:2122, 1923.

3. Zamorani: Riv. di. clin. pediat. **23**:1, 1925.

4. Knoepfelmacher, W., and Kohn, C.: Monatschr. f. Kinderh. **22**:1, 1921.

5. McNee, J. W.: Brit. M. J. **1**:716, 1922; Quart. J. Med. **16**:390, 1923; Brit. M. J. **2**:495, 1924; Med. Klin. **9**:1125, 1912; Quart. J. Med. **3**:221, 1909; J. Path. & Bact. **18**:325, 1915; **23**:342, 1920. McNee, J. W., and Keefer, C. S.: Brit. M. J. **2**:52, 1925.

hepatic; (2) toxic and infective hepatic, and (3) hemolytic. These three types may also be found in the new-born infant.

Obstructive Hepatic Jaundice.—A pure obstructive type is usually the result of congenital anomalies; these anomalies may consist of either a congenital obliteration of the bile passages, or congenital tumors around the porta hepatis, causing compression of the bile passages. This type of icterus always gives the direct van den Bergh reaction and usually appears only some time after birth. Bile, as a rule, is present in the urine.

Toxic and Infective Hepatic Jaundice.—(*a*) Icterus septicus, the most common type, next to icterus neonatorum, usually arises from an infection of the umbilicus. Birch-Hirschfeld,[6] who has made an extensive study of necropsies in such cases, demonstrated an acute interstitial and parenchymatous hepatitis in most instances. The clinical picture is that of sepsis together with icterus, bile in the urine and a direct van den Bergh reaction.

(*b*) Winckel's disease, or cyanosis afebralis icterica cum haemoglobinuria, was described by Winckel as the disease which occurs endemically and is characterized clinically by icterus, cyanosis, hemoglobinuria, and a normal or even subnormal temperature. The etiologic factor is probably infection.

(*c*) Another infective type of jaundice was described by Lesage and Demelin [7] and later by others occurring in connection with infections of the intestinal tract. The condition usually begins with an attack of cyanosis, sometimes with vomiting and convulsions, soon to be followed by diarrhea and icterus. The duration is about from three to twelve days. The mortality rate is high. Post mortem one usually finds an extensive catarrhal inflammation of the intestinal mucosa and a greater or lesser degree of atrophy and fatty degeneration of the liver.

(*d*) Icterus toxicus, from externally applied poisons, has occasionally been observed.

(*e*) Icterus occurring in connection with primary acute atrophy of the liver was reported in a few instances by Politzer,[8] Aufrecht [9] and Senator.[10]

Hemolytic Jaundice.—(*a*) Familial hemolytic jaundice, or anemia, occurs in the new-born infant as well as in the adult. In this group, too, probably belong most of the cases described as familial icterus neonatorum gravis. Some of these forms are called "Kernikterus" by the Germans. (*b*) Posthemorrhagic icterus was seen in a few

6. Birch-Hirschfeld: Virchows Arch. f. path. Anat. **87**:1, 1882.
7. Lesage and Demelin: Rev. de méd. **18**:1, 1898.
8. Politzer: Jahrb. f. Kinderh. **3**:40, 1860.
9. Aufrecht: Centralbl. f. inn. Med. **17**:273, 1896.
10. Senator: Wien. med. Presse, 1878, no. 17.

instances by Skormin [11] and Raudnitz.[12] (*c*) The literature on the subject of the etiology of icterus neonatorum simplex or physiologicus is enormous. A great number of theories have been advanced, some ingenious, some rather fantastic, but none satisfactory or proving the etiology of the condition.

THEORIES OF ICTERUS NEONATORUM

In general one can divide these theories into three main groups: (1) hepatogenous, (2) hematohepatogenous and (3) hematogenous.

Hepatogenous Theories.—These theories explain the icterus neonatorum either by mechanical disturbances in the bile flow or by disturbances of the circulation of the liver or of the liver cells themselves. Virchow,[13] in his later views, thought that a catarrhal swelling, or a plug, blocks the common duct. He made no differentiation between icterus neonatorum and icterus catarrhalis. Necropsy studies, however, did not substantiate these views. Quisiling [14] was the first who attempted to support Virchow's views. He found a block in the common duct in a 3 day old icteric child. Quisiling also thought that bacterial influence plays an important rôle. The same theory of bacterial influence was then further advanced by Czerny and Keller [15] who claimed that enteral infections are the chief cause of icterus neonatorum. They claimed that with the improved methods of asepsis and with the reduction of puerperal infections icterus neonatorum also becomes less common. They did not separate icterus neonatorum gravis from icterus neonatorum simplex, and considered the first condition merely as a more virulent infection. Unger,[16] in Vienna, observed 782 new-born infants and found icterus present in about 20.2 per cent; he also found that the majority of these icteric children also had dyspeptic enteric manifestations. Unger, therefore, came to the conclusion that the clinical proof for Czerny and Keller's theory was thus established.

Other authors believe that a pyemic or septic infection is the cause of icterus neonatorum (Abrami).[17] As we shall show later, there is no reason to consider infection as a factor in the production of icterus neonatorum, because icterus neonatorum is present in all new-born infants. Another group of authors ascribes icterus neonatorum to

11. Skormin: Jahrb. f. Kinderh. **56**:176, 1902.

12. Raudnitz: Prag. med. Wchnschr., 1884, no. 2.

13. Virchow: Arch. f. Path. Anat. u. Physiol., 1847, no. 1, pp. 379 and 407; Ges. Abhandlungen, pp. 850 and 858.

14. Quisiling: Arch. f. Kinderh. **7**:32, 1887.

15. Czerny and Keller: Des Kindes Ernaehrung, 1909, vol. 2, p. 204.

16. Unger, quoted by Ylppö (footnote 24).

17. Abrami: Les icteres infectieux d'origine septicémique et l'infection déscendente des voies biliaires, Thèse, Paris, 1910.

circulatory disturbances and changes. Frerich [18] thought that as a result of the stopping of the blood flow from the umbilical vein to the portal vein a negative pressure develops in the capillaries of the liver, and therefore bile overflows into the blood stream. Quinke [19] believed that the bile becomes reabsorbed from the intestines and is brought back through the portal vein to the liver, and if the ductus aurantii is open the bile will overflow into the general circulation. Some authors believe that the cause of icterus lies in disturbances of the normal function of the liver cells, while Knoepfelmacher [20] ascribed it to the stasis resulting from an increased viscoscity of the bile. Bassi and Chauffard [21] were the first to consider a functional disturbance of liver cells in the production of icterus in general. Minkowski [22] further advanced this idea. According to him, icterus arises either per stasin or per diapedesin, and the latter is the result of disturbances of the secretory function of the liver cells. Pick [23] has adopted these ideas for icterus neonatorum. Ylppö,[24] in his brilliant studies on icterus neonatorum, came to the conclusion that the liver at birth has not taken up its function completely, and since there is a physiologic increase of bile flow toward the end of the fetal period and after birth the bile overflows into the general circulation. An extensive study of necropsies of new-born infants was made by Birch-Hirschfeld,[6] who performed 600 examinations on new-born children. In the majority of cases he found edema of Glisson's capsule (which he thought was the result of stasis in the terminal part of the umbilical vein). He concluded that this edema causes compression of the bile capillaries and thus icterus. These necropsies, however, were made on infants who died of circulatory or respiratory disturbances, and these observations, therefore, can hardly be accepted for normal children. Other investigators, like Hasse,[25] could not confirm these observations.

Hematohepatogenous Theories.—As a basis for all hematohepatogenous theories it is assumed that in icteric new-born infants there is an increased destruction of red blood corpuscles, causing the liver to produce an excessive amount of viscid bile, some of which finds its way into the general circulation. Violet [26] believed that icterus results

18. Frerich: Klinik der Leberkrankheiten, 1858.

19. Quinke: Arch. f. exper. Path. u. Pharmakol. **19**:34, 1892.

20. Knoepfelmacher: Jahrb. f. Kinderh. **47**:447, 1898; Wien. med. Wchnschr. **20**:242, 1908; Jahrb. f. Kinderh. **67**:36, 1908.

21. Bassi and Chauffard, quoted by Ylppö (footnote 24).

22. Minkowski: Verhandl. d. Cong. f. inn. Med., 1900, p. 136.

23. Pick: Wien. klin. Wchnschr. **5**:307, 1892.

24. Ylppö: Ztschr. f. Kinderh. **9**:208 and 314, 1913; **17**:334, 1918; Eulenburgs Real-Enzyklopaedie, vol. 5.

25. Hasse: Jahrb. f. Kinderh. **69**:625, 1909.

26. Violet: Arch. f. path. Anat. **80**:353, 1880.

from the excess of blood entering the child's circulation from the placenta at the moment of birth. The excess, he thinks, is hemolyzed by the infant. Hofmeier [27] explained the excessive destruction of blood by insufficient nutrition which leads to the consumption of body protein, and the first protein to be used up is the circulating protein —the protein of the red blood corpuscles.

Hematogenous Theories.—The first theories of icterus neonatorum were hematogenous. Virchow,[18] in his earlier views, was the first who thought that icterus developed from excessive destruction of red blood corpuscles, liberating hemoglobin which is changed into hematoidin, an isomere of bilirubin, giving rise to icterus. Although he later abandoned these views he was still the first to suggest the true nature of icterus neonatorum. Others, like Schulze [28] and Zweifel,[29] thought that the child develops subcutaneous hemorrhages during the process of labor (giving the child the red appearance), and thus giving rise to the formation of bilirubin. Some found an increased fragility of the red blood corpuscles (Chatala and Daunay,[30] Leuret and Monssons [31]) which, however, was not confirmed by Mensi,[32] Schlingenberg [33] or Mitchell.[34] The hematogenous theories, however, were almost completely abandoned when Minkowski and Naunyn,[35] in 1866, published the results of experiments on geese with extirpated liver. They were unable to produce icterus in these animals. These experiments led to the formulation of the maxim, "no icterus without liver." Not before the recognition of the importance of the function of the reticulo-endothelial system in bile formation and not before the publications of van den Bergh,[1] McNee [5] and Lepehne [36] on icterus in general was the truth of this statement doubted. It is therefore important to outline briefly what has been done in the past twenty years with regard to the question of hemolytic jaundice in general.

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27. Hofmeier: Ztschr. f. Geburtsh. u. Gynäk. **13**:287, 1886.

28. Schulze: Arch. f. path. Anat. **81**:175, 1880.

29. Zweifel: Untersuchungen ueber den Verdaungsapparat der Neugeborenen, Berlin, A. Hirschwald, 1874.

30. Chatala and Daunay: Obstétrique, December, 1908; Compt. rend. Soc. de biol. **64**:801, 1908.

31. Leuret and Monssons, quoted by Ylppö (footnote 24).

32. Mensi, quoted by Ylppö (footnote 24).

33. Schlingenberg: Med. Tijdschr. v. Geneesk. **2**:1593, 1910.

34. Mitchell, J. McK.: The Rôle of Hemolysis in Jaundice of the New-Born Infant, Am. J. Dis. Child. **36**:486 (Sept.) 1928.

35. Minkowski and Naunyn: Arch. f. exper. Path. u. Pharmakol. **21**:1, 1866.

36. Lepehne, G.: Zieglers Beitr. z. path. Anat. u. z. allg. Path. **64**:55, 1918; München. med. Wchnschr. **66**:619, 1919; Deutsches Arch. f. klin. Med. **132**:96, 1920; **135**:79, 1921; **136**:88, 1921.

THE IMPORTANCE OF THE RETICULO-ENDOTHELIAL SYSTEM WITH REGARD TO BILE FORMATION

The term "reticulo-endothelial system" was introduced by Aschoff [37] in 1904. Aschoff and his pupils, especially Kiyono,[38] recognized the fact that the cells of that system were able to break down hemoglobin after taking up the red blood corpuscles by phagocytosis. Hemosiderin, the iron containing portion, can be demonstrated in these cells (Prussian blue reaction), and thus a precursor of bilirubin or anhepatic bilirubin is formed. Not all of the cells of the system, however, show this ability. In man and higher animals the endothelial cells of the spleen play the preponderating rôle, while in birds the Kupffer cells of the liver are mostly concerned with the breaking down of the red blood corpuscles. In 1912, McNee [5] repeated the experiments of Minkowski and Naunyn,[35] finding the same results, but recognizing that in birds one deals with an absolutely different set of circumstances, the liver being large and the spleen small and poorly developed. Kupffer's cells occur in large numbers in birds, but are relatively few in man and in higher animals. Lepehne [36] further developed these experiments in 1917. Working first on pigeons, he confirmed the observations of McNee.[5] He then transferred his experiments to rats, who have large spleens and scanty Kupffer cells. He concluded that in the higher animals and in man the function of the breaking down of red corpuscles is exercised by the spleen. The reticulo-endothelial system is thus shown to be of the greatest importance in the formation of bilirubin.

THE VAN DEN BERGH REACTION

Van den Bergh, who introduced the Ehrlich diazo reaction as a qualitative and quantitative test for even minute quantities of bilirubin, was able to demonstrate that there are two types of bilirubin present. One type, giving the indirect positive reaction, arises from the bilirubin (precursor of bilirubin) which is formed by the reticulo-endothelial system and has not passed through the liver cells. A second type, which gives the direct immediate reaction, arises from bilirubin which has passed through the liver. Summarizing, we may say that bile pigment can be formed outside the liver. In man and in higher animals the spleen is the chief factor in the production of hemolytic jaundice. We have felt, therefore, that from the standpoint of the new conceptions of the origin of icterus, particularly hemolytic icterus, a study of icterus neonatorum should be made.

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37. Aschoff, L.: München. med. Wchnschr. **69**:1352, 1922.

38. Kiyono: Die vietale Kraminspeiecherung, Jena, 1914.

HEMOLYSIS

In the course of some recent work which entailed the study of blood taken from the umbilical cord, we observed that practically all samples showed hemolysis in the serum. This led us to believe that there must be some relationship between this tendency to early hemolysis and icterus neonatorum. The greatest care in collecting cord blood was exercised; absolutely dry test tubes were used as well as a dry needle and syringe. The cord was carefully wiped dry and the needle inserted into the umbilical vein. All samples of blood were obtained at the delivery, immediately after the cord was cut and before the delivery of the placenta. Most serums showed hemolysis even though they were separated off immediately, while those which did not show hemolysis at once developed a hemolytic tinge after standing for

TABLE 1.—*The Result of Red Blood Cell Counts Made on Oxalated Cord Blood at Intervals; All Samples Show a Rapid Diminution in the Number of Red Blood Cells, While the Normal Adult Control Shows Only Slight Variations*

Case	Birth	12 Hours	24 Hours	36 Hours	48 Hours	72 Hours	96 Hours	120 Hours	144 Hours	264 Hours
33	6,450,000	5,800,000	4,200,000	2,380,000	1,550,000	300,000	0	0	0	0
34	7,350,000	6,800,000	5,100,000	3,900,000	2,100,000	800,000	200,000	0	0	0
35	7,100,000	6,050,000	4,950,000	3,850,000	2,200,000	700,000	0	0	0	0
36	6,450,000	5,800,000	4,600,000	3,200,000	2,000,000	500,000	0	0	0	0
37	6,600,000	5,450,000	4,380,000	3,500,000	1,700,000	600,000	0	0	0	0
38	5,900,000	5,700,000	5,600,000	5,600,000	4,500,000	3,800,000	1,800,000	800,000	0	0
39	6,200,000	5,900,000	4,800,000	3,600,000	2,000,000	800,000	100,000	0	0	0
40	6,800,000	5,700,000	4,600,000	3,200,000	1,500,000	550,000	0	0	0	0
41	7,300,000	6,500,000	5,100,000	3,700,000	2,800,000	1,300,000	0	0	0	0
42	5,300,000	5,000,000	4,800,000	4,600,000	4,400,000	3,800,000	3,050,000	2,150,000	1,100,000	0
*	4,900,000	4,900,000	4,850,000	4,850,000	4,820,000	4,800,000	4,780,000	4,700,000	4,700,000	4,600,000

* Normal adult control.

several hours in contact with the corpuscles. Samples of oxalated cord blood were allowed to stand in a test tube in a refrigerator, and red cell counts were made at intervals. It was found that the counts rapidly dimished so that at the end of three or four days all the red cells had hemolyzed away. Control samples of oxalated adult blood showed only slight variations over a period of eleven days.

Table 1 shows the red cell counts made in this way, with ten samples of cord blood and one of an adult as control. At the end of ninety-six hours, only four samples showed any unhemolyzed cells; at one hundred and twenty hours only two samples showed unhemolyzed cells, while at the end of one hundred and forty-four hours, only one of the samples had any cells remaining. Chart 1 shows the red cell counts of: (1) peripheral blood from a new-born infant; (2) cord blood from the same infant, oxalated and standing in a refrigerator, and (3) a control from a normal adult. The infant's peripheral blood shows the early rapid fall in the number of red blood cells from 6,900,000 at birth to 4,250,000 in one hundred and eight hours, with a

subsequent rise to nearly 4,500,000, while in the oxalated cord blood the cells were completely hemolyzed at the end of the ninety-six hours. The control sample from the adult showed only slight variations during the period of observation.

FRAGILITY

Studies were made on thirty-nine samples of cord blood. Thirty-seven of these showed an increase of fragility, in all but two of which the hemolysis began at or near the isotonic solution. It is curious to note that even when hemolysis was present in isotonic saline, it was never complete before the use of solutions of from 0.45 to 0.3 per cent. Chart 2 shows: (1) the average curve of fragility—thirty-eight

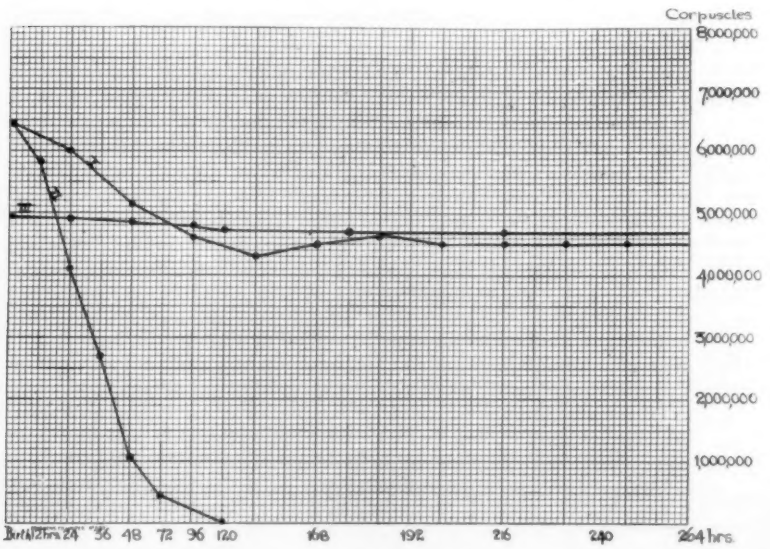

Chart 1.—*I*, red blood cell counts in the infant; *II*, red blood cell counts in cord blood standing, and *III*, red blood cell counts in normal blood standing.

samples of cord blood, and (2) the average curve in twenty-five control samples from adults. It will be seen that in cord blood 4 per cent of the cells are hemolyzed in 0.8 per cent saline, but that the hemolysis is not complete before the administration of 0.3 per cent, or the same dilution in which it is complete in normal blood. If the cord blood is examined at intervals for fragility, it is found that the fragility increases the longer the intervals. Chart 3 shows hemolysis curves of the samples of blood done at birth and after twenty-four, seventy-two and ninety-six hours' standing. It will be seen that the point of complete hemolysis advances the longer the blood is allowed to stand; control blood showed only slight variation in fragility in the same period.

We have exchanged serums of mother and child in ten instances without in any way altering the fragility. The maternal corpuscles showed normal resistance, while those of the cord blood showed the same fragility as without the mother's serum. Mitchell [34] claimed that there is a hemolysin in maternal blood against the infants' corpuscles, but he would doubtless have found his samples of cord blood equally hemolytic without the addition of the maternal serum. Table 2 and chart 4 amply demonstrate that no alteration in fragility results from exchange of serums. Ten cases were studied, the details of which are given in table 2. In chart 4 it will be seen that the identical curve results when the cord blood is examined for fragility at birth, after

TABLE 2.—*Results of Studies on Ten Cases*

	Fragility of Red Blood Cells in																	
	Cord Blood at Birth		Cord Blood After 24 Hours Standing		Cord Blood After Exposure to Physiologic Solution of Sodium Chloride for 24 Hours		Cord Blood After Exposure to Mother's Serum for 1 Hour		Cord Blood After Exposure to Mother's Serum for 24 Hours		Mother's Blood		Mother's Blood After 24 Hours Standing		Mother's Blood After Exposure to Cord Serum for 1 Hour		Mother's Blood After Exposure to Cord Serum for 24 Hours	
Case	Starting	Complete	Starting	Complete	Starting	Complete	Starting	Complete	Starting	Complete	Starting	Complete	Starting	Complete	Starting	Complete	Starting	Complete
33	0.8	0.35	0.8	0.4	0.8	0.4	0.8	0.35	0.8	0.4	0.4	0.3	0.4	0.3	0.4	0.3	0.4	0.3
34	0.8	0.35	0.8	0.4	0.8	0.4	0.8	0.35	0.8	0.4	0.4	0.3	0.4	0.3	0.4	0.3	0.4	0.3
35	0.8	0.35	0.8	0.35	0.8	0.35	0.8	0.35	0.8	0.4	0.4	0.3	0.4	0.3	0.4	0.3	0.4	0.3
36	0.8	0.35	0.8	0.4	0.8	0.4	0.8	0.35	0.8	0.35	0.4	0.3	0.4	0.3	0.4	0.3	0.4	0.3
37	0.8	0.35	0.8	0.4	0.8	0.4	0.8	0.35	0.8	0.4	0.4	0.3	0.4	0.3	0.4	0.3	0.4	0.3
38	0.6	0.35	0.8	0.4	0.8	0.4	0.6	0.35	0.8	0.4	0.4	0.3	0.4	0.3	0.4	0.3	0.4	0.3
39	0.6	0.35	0.7	0.4	0.7	0.4	0.6	0.35	0.7	0.4	0.4	0.3	0.4	0.3	0.4	0.3	0.4	0.3
40	0.7	0.35	0.8	0.4	0.8	0.4	0.7	0.35	0.8	0.4	0.4	0.3	0.4	0.3	0.4	0.3	0.4	0.3
41	0.8	0.35	0.8	0.4	0.8	0.4	0.8	0.35	0.8	0.4	0.4	0.3	0.4	0.3	0.4	0.3	0.4	0.3
42	0.7	0.35	0.8	0.4	0.8	0.4	0.7	0.35	0.8	0.4	0.4	0.3	0.4	0.3	0.4	0.3	0.4	0.3

exposure to the maternal serum and after exposure to physiologic solution of sodium chloride. No effect of the cord serum on the maternal corpuscles nor of the maternal serum on the cord blood corpuscles could be demonstrated. The changes occurring in these experiments at the end of six hours were identical with the observations in chart 3.

FRAGILITY OF THE PERIPHERAL BLOOD IN THE NEW-BORN INFANT

The fragility of the peripheral blood was studied in twenty new-born infants. Tests were made beginning at birth and at intervals of forty-eight hours until the resistance was found to be normal. The combined and micro-macro method of Waugh and Chase [39] was used. Fragility was increased at birth in nineteen of the twenty cases. At

39. Waugh and Chase: J. Lab. & Clin. Med. **13**:872, 1928.

the end of one week the resistance was slightly greater than normal in all but two of the infants who still showed a slight increase of fragility. Chart 5 shows the average fragility of the red cells of the peripheral blood in the twenty cases at birth and at the end of one week and an average curve of ten normal adults.

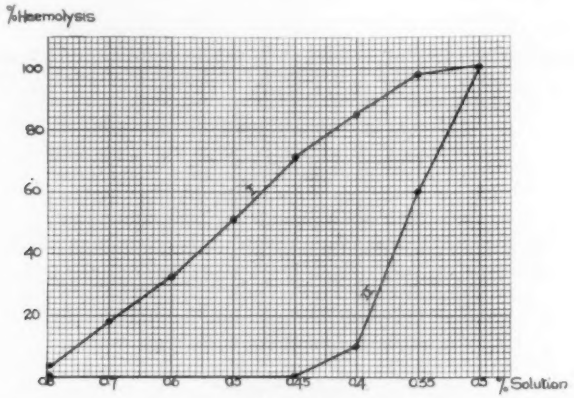

Chart 2.—*I* represents the average fragility of red blood cells in cord blood in thirty-eight cases; *II*, average fragility in adult (normal) blood in twenty-five cases.

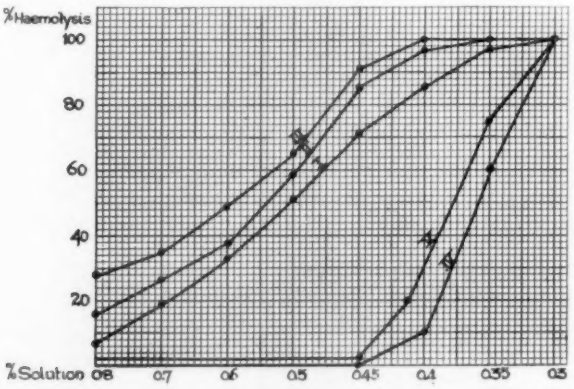

Chart 3.—*I*, fragility of red blood cells in cord blood at birth; *II*, after twenty-four hours' standing; *III*, after ninety-six hours' standing; *IV*, fragility of red blood cells in adult (normal) blood; *V*, after ninety-six hours' standing.

NUCLEATED AND RETICULATED RED BLOOD CELLS

Counts made from fresh smears showed a great increase in both these types of cells at birth with a rapid decline ending with the first week of life. The number of nucleated red blood cells varied at birth from 600 to 1,100 per million erythrocytes. At the end of the first week the number fell to between from 25 to 50 per million. Reticulated cells at birth numbered from 5 to 12 per high power field (normal

from 2 to 4 per high power field). At the end of the first week of life these cells almost entirely disappeared (table 4). Chart 6 represents: (1) the red blood counts in an infant during the first eleven days of life, (2) nucleated red cell counts and (3) the reticulated red cell counts during this period.

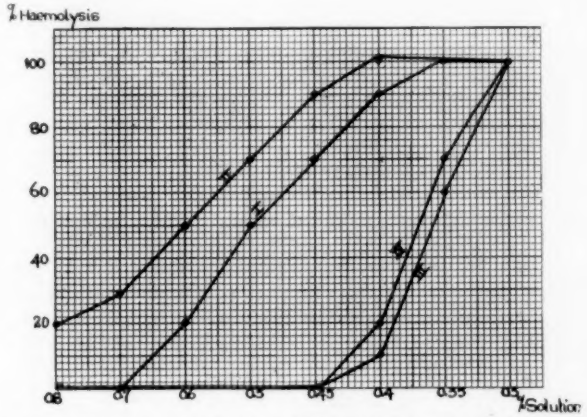

Chart 4.—*I* represents the fragility of red blood cells in cord blood at birth, after exposure to mother's serum for one hour and after exposure to physiologic solution of sodium chloride for one hour; *II*, fragility in red blood cells in cord blood standing for twenty-four hours; red blood cells exposed to mother's serum for twenty-four hours, and kept in physiologic solution of sodium chloride for twenty-four hours; *III*, fragility of red blood cells in mother's blood immediately after taking; after exposure to cord serum for one hour, and after exposure to physiologic solution of sodium chloride for one hour; *IV*, fragility of red blood cells in mother's blood standing twenty-four hours; red blood cells exposed to cord serum for twenty-four hours, and kept in physiologic solution of sodium chloride for twenty-four hours.

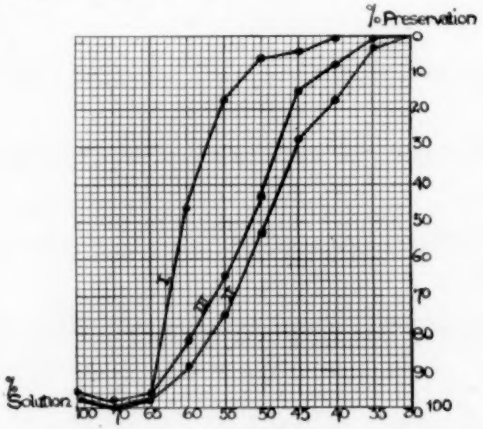

Chart 5.—*I* represents the average fragility of red blood cells at birth in twenty cases; *II*, average fragility of red blood cells at the end of one week in twenty cases; *III*, average fragility in adult normal blood in ten cases.

TABLE 3.—*Fragility Experiments on Unhemolized Fractions*

Case	Sodium Chloride Solution, per Cent	Fragility of Red Blood Cells: Fragility Immediately After Birth	Fragility of Red Blood Cells: Fragility of Unhemolized Fractions: 0.8 per Cent	0.7 per Cent	0.6 per Cent	0.5 per Cent	0.45 per Cent	0.4 per Cent	Number of Nucleated Red Blood Cells Remaining in Unhemolized Fractions	Number of Reticulated Red Blood Cells Remaining in Unhemolized Fractions	Number of Nucleated Red Blood Cells in Peripheral Blood of Infant During First Week of Life	Number of Reticulated Red Blood Cells in Peripheral Blood of Infant During First Week of Life
30	0.8	10	0	0	0	0	0	0	500	6	600 birth	7 birth
	0.7	20	10	0	0	0	0	0	430	5	550 1 day after birth	6 1 day after birth
	0.6	30	30	20	0	0	0	0	400	3	450 2 days after birth	5 2 days after birth
	0.5	50	50	50	50	0	0	0	200	0-1	320 3 days after birth	3 3 days after birth
	0.45	70	70	70	70	50	0	0	50	0	130 4 days after birth	1-2 4 days after birth
	0.4	90	90	90	90	90	70	0	20–25	0	50 6 days after birth	0-1 6 days atfer birth
	0.35	100	100	100	100	100	100	90	0	0	48 9 days after birth	0-1 9 days atfer birth
	0.3	100	100	100	100	100	100	100	0	0		
33	0.8	10	0	0	0	0	0	0	350	5	400 birth	7 birth
	0.7	20	10	0	0	0	0	0	275	4	350 1 day after birth	6 1 day after birth
	0.6	30	30	20	0	0	0	0	185	2	210 2 days after birth	4 2 days after birth
	0.5	60	60	60	50	0	0	0	80	0-1	130 3 days after birth	2 3 days after birth
	0.45	70	70	70	70	50	0	0	60	0	90 4 days after birth	1 4 days after birth
	0.4	90	90	90	90	90	60	0	50	0	75 5 days after birth	0-1 5 days after birth
	0.35	100	100	100	100	100	100	100	0	0	50 6 days after birth	0 6 days after birth
	0.3	100	100	100	100	100	100	100	0	0	35 7 days after birth	0 7 days after birth
34	0.8	20	0	0	0	0	0	0	800	7	1000 birth	10 birth
	0.7	30	20	0	0	0	0	0	620	5	800 1 day after birth	7 1 day after birth
	0.6	40	40	30	0	0	0	0	500	4	690 2 days after birth	5 2 days after birth
	0.5	50	50	50	30	0	0	0	250	2	400 3 days after brith	3 3 days after birth
	0.45	70	70	70	70	40	0	0	85	0-1	150 5 days after birth	0-1 5 days after birth
	0.4	90	90	90	90	90	60	0	55	0	75 8 days after birth	0 8 days after birth
	0.35	100	100	100	100	100	100	100	0	0	25 10 days after birth	0 10 days after birth
	0.3	100	100	100	100	100	100	100	0	0		
35	0.8	10	0	0	0	0	0	0	930	8	1100 birth	10 birth
	0.7	20	10	0	0	0	0	0	700	5	930 1 day after birth	8 1 day after birth
	0.6	30	30	20	0	0	0	0	510	3	720 2 days after birth	6-7 2 days after birth
	0.5	50	50	50	30	0	0	0	265	1	480 3 days after birth	5 3 days after birth
	0.45	80	80	80	80	80	0	0	90	0-1	335 5 days after birth	2 5 days after birth
	0.4	90	90	90	90	90	60	0	35	0	110 7 days after birth	0-1 7 days after birth
	0.35	100	100	100	100	100	100	100	0	0	55 9 days after birth	0 9 days after birth
	0.3	100	100	100	100	100	100	100	0	0		
36	0.8	20	0	0	0	0	0	0	410	4	650 birth	6 birth
	0.7	30	20	0	0	0	0	0	285	2	525 1 day after birth	4 1 day after birth
	0.6	40	40	20	0	0	0	0	135	0-1	390 2 days after birth	3 2 days after birth
	0.5	60	60	60	50	0	0	0	85	0	220 3 days after birth	0-1 3 days after birth
	0.45	80	80	80	80	70	0	0	30	0	120 4 days after birth	0 4 days after birth
	0.4	90	90	90	90	90	90	0	15	0	65 7 days after birth	0 7 days after birth
	0.35	100	100	100	100	100	100	100	0	0	35 10 days after birth	0 10 days after birth
	0.3	100	100	100	100	100	100	100	0	0		

37	0.8	20	0	0	0	0	0	0	520	6	700	birth	8	birth
	0.7	30	20	0	0	0	0	0	435	4	550	1 day after birth	6	1 day after birth
	0.6	40	30	30	0	0	0	0	240	2	410	2 days after birth	4	2 days after birth
	0.5	50	50	50	40	0	0	0	160	0-1	340	3 days after birth	2	3 days after birth
	0.45	70	70	70	70	50	0	0	90	0	210	4 days after birth	0-1	4 days after birth
	0.4	90	90	90	90	90	70	0	40	0	80	6 days after birth	0	6 days after birth
	0.35	100	100	100	100	100	100	100	0	0	20	8 days after birth	0	8 days after birth
	0.3	100	100	100	100	100	100	100	0	0				
38	0.8	0	0	0	0	0	0	0	500	6	500	birth	6	birth
	0.7	0	0	0	0	0	0	0	500	6	430	1 day after birth	4	1 day after birth
	0.6	20	20	20	0	0	0	0	380	4	320	2 days after birth	2	2 days after birth
	0.5	50	50	50	50	0	0	0	290	2	125	4 days after birth	0-1	4 days after birth
	0.45	70	70	70	70	50	0	0	115	0-1	45	6 days after birth	0	6 days after birth
	0.4	90	90	90	90	90	70	0	42	0	15	9 days after birth	0	9 days after birth
	0.35	100	100	100	100	100	100	100	0	0				
	0.3	100	100	100	100	100	100	100	0	0				
39	0.8	0	0	0	0	0	0	0	650	7	650	birth	7	birth
	0.7	0	0	0	0	0	0	0	650	7	525	1 day after birth	5	1 day after birth
	0.6	20	20	20	0	0	0	0	400	5	410	2 days after birth	3	2 days after birth
	0.5	50	50	50	50	0	0	0	210	3	300	3 days after birth	1	3 days after birth
	0.45	70	70	70	70	50	0	0	115	1	50	6 days after birth	0	6 days after birth
	0.4	90	90	90	90	90	70	0	45	0	20	9 days after birth	0	9 days after birth
	0.35	100	100	100	100	100	100	100	0	0				
	0.3	100	100	100	100	100	100	100	0	0				
40	0.8	0	0	0	0	0	0	0	800	7	800	birth	7	birth
	0.7	20	20	0	0	0	0	0	600	5	650	1 day after birth	5	1 day after birth
	0.6	40	40	40	0	0	0	0	410	2	525	2 days after birth	3	2 days after birth
	0.5	50	50	50	50	0	0	0	280	1	410	3 days after birth	2	3 days after birth
	0.45	70	70	70	70	50	0	0	145	0-1	290	4 days after birth	0-1	4 days after birth
	0.4	90	90	90	90	90	70	0	55	0	175	5 days after birth	0	5 days after birth
	0.35	100	100	100	100	100	100	100	0	0	50	7 days after birth	0	7 days after birth
	0.3	100	100	100	100	100	100	100	0	0	20	11 days after birth	0	11 days after birth
41	0.4	20	0	0	0	0	0	0	800	9	1000	birth	12	birth
	0.7	30	20	0	0	0	0	0	640	6	800	1 day after birth	10	1 day after birth
	0.6	40	40	40	0	0	0	0	480	4	570	2 days after birth	7	2 days after birth
	0.5	60	60	60	40	0	0	0	310	1	310	4 days after birth	4	4 days after birth
	0 45	70	70	70	70	50	0	0	159	0	100	6 days after birth	1	6 days after birth
	0.4	90	90	90	90	90	70	0	85	0	60	8 days after birth	0-1	8 days after birth
	0.35	100	100	100	100	100	100	100	0	0	20	9 days after birth	0	9 days after birth
	0.3	100	100	100	100	100	100	100	0	0				
42	0.8	0	0	0	0	0	0	0	350	5	350	birth	5	birth
	0.7	10	10	0	0	0	0	0	210	3	200	1 day after birth	3	1 day after birth
	0.6	30	30	30	0	0	0	0	120	1	120	2 days after birth	1	2 days after birth
	0.5	50	50	50	50	50	0	0	70	0-1	65	4 days after birth	0-1	4 days after birth
	0.45	70	70	70	70	70	0	0	25	0	35	6 days after birth	0	6 days after birth
	0.4	90	90	90	90	90	70	0	10	0	20	8 days after birth	0	8 days after birth
	0.35	100	100	100	100	100	100	100	0	0				
	0.3	100	100	100	100	100	100	100	0	0				

The unhemolyzed fractions in our fragility experiments were studied to see which cells hemolyzed first and which were more resistant. Counts made of the cells remaining in each test tube after hemolysis had taken place showed that the reticulated cells were the first to hemolyze. They disappeared completely in a solution of about 0.5 per cent saline. The nucleated red cells disappeared somewhat more slowly. In solutions of 0.4 per cent saline there were from 20 to 25 nucleated red cells per million as compared with 500 per million in the first tube of 0.8 per cent saline. The residual cells remaining in each

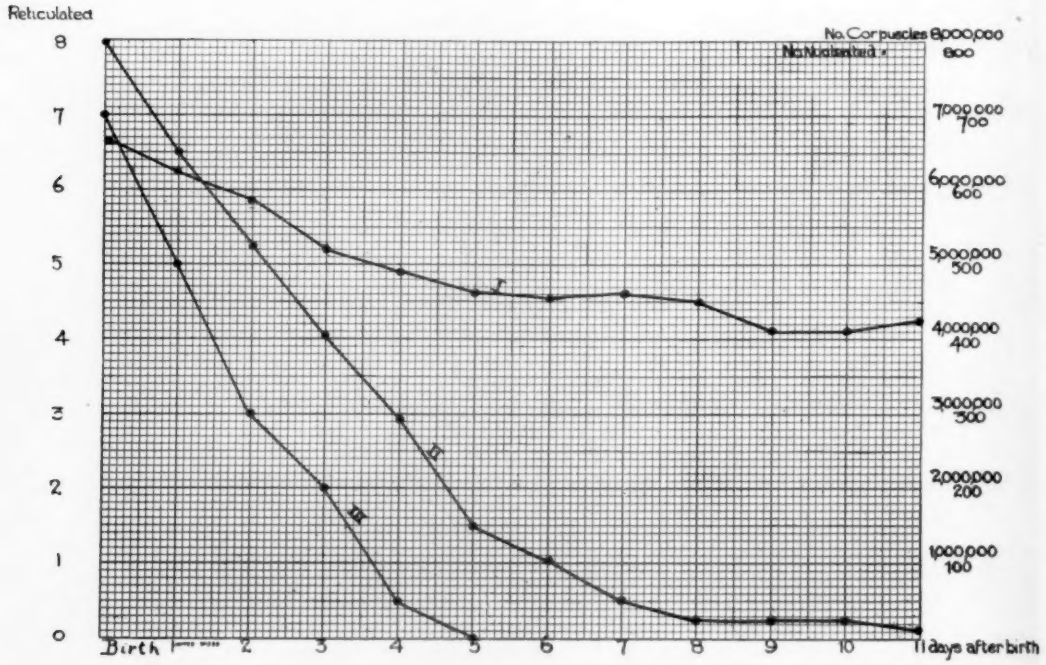

Chart 6.—*I* represents the red blood cell counts in an infant during the first eleven days of life; *II*, the nucleated red blood counts during the first eleven days of life, and *III*, the reticulated red blood cell counts during the same period.

tube were set up again in series beginning at 0.8 per cent saline. These revealed, as was expected, that the remaining cells all showed an increasing resistance, so that the cells remaining in the 0.45 test tube showed a nearly normal curve. It seems then that the more immature cells are the ones most sensitive to hypotonic saline, and that when these cells have hemolyzed the remaining cells show normal curves (table 3). Table 3 also shows that the return of the fragility of the red blood cells to normal as shown in chart 5—coincides with the disappearance of these immature cells from the peripheral circulation.

TABLE 4.—*Observation on van den Bergh Reaction and Icteric Index*

Case	Fragility: Cord Blood: Immediately After Taking: Starting	Fragility: Cord Blood: Immediately After Taking: Complete	Fragility: Cord Blood: Standing: Starting	Fragility: Cord Blood: Standing: Complete	Fragility: Infant Blood: Birth	Fragility: Infant Blood: End of One Week	Fragility: Normal Adult Blood: Immediately After Taking: Starting	Fragility: Normal Adult Blood: Immediately After Taking: Complete	Fragility: Normal Adult Blood: Standing: Starting	Fragility: Normal Adult Blood: Standing: Complete	Red Blood Counts: Birth	Red Blood Counts: End of One Week	Nucleated Red Blood Cells per 1,000,000: Birth	Nucleated Red Blood Cells per 1,000,000: End of 1 Wk.	Reticulated Red Blood Cells per High Power Field: Birth	Reticulated Red Blood Cells per High Power Field: End of 1 Wk.	Hemoglobin, per Cent: Birth	Hemoglobin, per Cent: End of 1 Wk.	Van den Bergh Reaction: Direct	Van den Bergh Reaction: Indirect	Van den Bergh Reaction: Quantitative Units	Icteric Index: Birth	Icteric Index: End of One Week	Icterus	Comment
1	0.8	0.35	...	....	.....	.....	0.4	0.3	0.4	0.3	.....	.....	...	...	..	..	...	...	—	—	...	..	..	0	
2	0.8	0.5	...	....	.....	.....	0.4	0.3	0.4	0.3	.....	.....	...	...	..	..	...	...	—	—	...	..	..	0	
3	0.8	0.4	...	....	.....	.....	0.4	0.3	0.4	0.3	.....	.....	...	...	..	..	...	...	—	—	...	..	..	0	
4	0.8	0.4	...	....	.....	.....	0.4	0.3	0.4	0.3	.....	.....	...	...	..	..	...	...	—	—	...	..	..	0	
5	0.8	0.35	...	....	.....	.....	0.4	0.3	0.4	0.3	.....	.....	...	...	..	..	...	...	—	—	...	..	..	0	
6	0.45	0.35	...	....	.....	.....	0.4	0.3	0.4	0.3	.....	.....	...	...	..	..	...	...	—	—	...	..	..	+	
7	0.8	0.35	0.8	0.35	.....	.....	0.4	0.3	0.4	0.3	7,100,000	.....	...	...	..	..	110	...	—	+	3	..	..	0	
8	0.8	0.35	0.5	0.35	.....	.....	0.4	0.3	0.4	0.3	5,100,000	4,500,000	...	...	..	..	98	...	—	+	4	..	..	0	
9	0.5	0.35	0.8	0.4	.....	.....	0.4	0.3	0.4	0.3	7,300,000	4,600,000	...	...	..	..	110	...	—	+	5	..	..	+	
10	0.8	0.35	...	....	.....	.....	0.4	0.3	0.4	0.3	6,500,000	4,250,000	...	...	..	..	106	...	—	+	3½	..	..	0	2d child of twins
11	...	....	...	....	Increased 3d day	.....	0.4	0.3	0.4	0.3	.....	.....	...	...	..	..	...	...	—	+	6	..	..	+	Infant, aged 3 da.
12	0.4	0.3	0.8	0.35	.....	.....	0.4	0.3	0.4	0.3	5,300,000	4,050,000	...	...	..	..	98	...	—	+	4½	..	..	+	
13	0.8	0.35	0.8	0.4	.....	.....	0.4	0.3	0.4	0.3	5,400,000	3,900,000	...	...	..	..	100	...	—	+	3	..	..	0	
14	0.45	0.3	0.8	0.35	.....	.....	0.4	0.3	0.4	0.3	7,100,000	4,800,000	...	...	..	..	108	...	—	+	5	..	..	+	
15	0.45	0.3	0.8	0.35	.....	.....	0.4	0.3	0.4	0.3	6,800,000	4,100,000	...	...	..	..	106	94	—	+	4	..	..	+	
16	0.7	0.35	0.8	0.4	.....	.....	0.4	0.3	0.4	0.3	.....	.....	...	...	..	..	...	...	—	+	3½	..	..	0	
17	0.7	0.35	0.8	0.4	.....	.....	0.4	0.3	0.4	0.3	.....	.....	...	...	..	..	...	...	—	+	7	..	..	+	
18	0.7	0.35	0.8	0.4	.....	.....	0.4	0.3	0.4	0.3	6,300,000	4,300,000	...	...	..	..	106	94	—	+	3½	..	..	0	
19	...	....	...	....	.....	.....	0.4	0.3	0.4	0.3	.....	.....	...	...	..	..	...	...	—	—	...	..	..	0	Man, 55; diabetes
20	...	....	...	....	.....	.....	0.4	0.3	0.4	0.3	.....	.....	...	...	..	..	...	...	—	—	...	..	..	0	Woman, 58; "
21	...	....	...	....	.....	.....	0.4	0.3	0.4	0.3	.....	.....	...	...	..	..	...	...	—	—	...	..	..	0	Woman, 35; "
22	...	....	...	....	.....	.....	0.4	0.3	0.5	0.3	.....	.....	...	...	..	..	...	...	—	—	...	..	..	0	Woman, 45; "
23	0.8	0.35	0.8	0.35	Increased	Normal	0.4	0.3	0.4	0.3	7,100,000	3,500,000	500	100	..	..	108	96	—	+	5	16	18	+	
24	0.8	0.35	0.8	0.6	Increased	Normal	0.4	0.3	0.4	0.3	6,900,000	5,000,000	800	50	..	..	108	98	—	+	6	16	18	+	
25	0.8	0.35	0.8	0.5	.....	.....	0.4	0.3	0.4	0.3	6,250,000	.....	700	...	..	..	102	...	—	+	3	8	..	0	Spina bifida
26	0.8	0.35	0.8	0.5	Increased	Normal	0.4	0.3	0.4	0.3	6,400,000	4,900,000	900	70	..	..	108	100	±	+	5½	17	18	+	1st child/twins
27	0.8	0.35	0.8	0.5	Increased	Normal	0.4	0.3	0.4	0.3	6,450,000	4,800,000	800	125	..	..	108	98	—	+	5½	17	18	+	2d child\
28	0.7	0.35	0.8	0.45	Increased	Normal	0.4	0.3	0.4	0.3	6,800,000	4,700,000	300	35	..	..	104	98	—	+	4	9	6	0	
29	0.7	0.35	...	....	Increased	Normal	0.4	0.3	0.4	0.3	6,900,000	4,400,000	700	75	8	0	108	98	—	+	3½	8	4	0	
30	0.8	0.35	...	....	Increased	Normal	0.4	0.3	0.4	0.3	7,300,000	4,400,000	600	48	7	0-1	110	98	—	+	5	18	19	+	
31	0.6	0.3	0.8	0.35	Normal	Normal	0.4	0.3	0.4	0.3	5,400,000	3,930,000	300	25	5	0	98	90	—	+	3	7	5	0	
32	0.8	0.35	...	....	Increased	Normal	0.4	0.3	0.4	0.3	7,300,000	4,800,000	950	75	10	0-1	110	98	—	+	5	18	19	+	
33	0.8	0.35	...	....	Increased	Normal	0.4	0.3	0.4	0.3	6,450,000	4,500,000	400	20	7	0	102	94	—	+	3	10	6	0	
34	0.8	0.35	...	....	Increased	Normal	0.4	0.3	0.4	0.3	7,350,000	4,200,000	1000	25	10	0	112	94	—	+	7	20	24	+	
35	0.8	0.35	0.8	0.35	Increased	Normal	0.4	0.3	0.4	0.3	7,100,000	4,550,000	1100	55	10	0	114	96	—	+	8	20	30	+	
36	0.8	0.35	0.8	0.4	Increased	Normal	0.4	0.3	0.4	0.3	6,450,000	4,000,000	650	35	6	0	108	92	—	+	6	18	20	+	1st child/twins
37	0.8	0.35	0.8	0.4	Increased	Normal	0.4	0.3	0.4	0.3	6,600,000	4,400,000	700	20	8	0	108	94	—	+	6	19	21	+	2d child\
38	0.6	0.35	0.8	0.4	Increased	Normal	0.4	0.3	0.4	0.3	5,900,000	4,700,000	500	15	6	0	104	96	—	+	3	10	7	0	
39	0.6	0.35	0.7	0.4	Increased	Normal	0.4	0.3	0.4	0.3	6,200,000	4,300,000	650	20	7	0	106	98	—	+	3½	11	6	0	
40	0.7	0.35	0.8	0.4	Increased	Increased	0.4	0.3	0.4	0.3	6,800,000	4,600,000	800	50	7	0	110	98	—	+	4	14	15	?	
41	0.8	0.35	0.8	0.4	Increased	Increased	0.4	0.3	0.4	0.3	7,300,000	4,550,000	1000	20	12	0	114	96	—	+	8	28	30	+	
42	0.7	0.35	0.8	0.4	Increased	Normal	0.4	0.3	0.4	0.3	5,300,000	4,800,000	350	20	5	0	100	96	—	+	2½	8	3	0	
43	0.8	0.35	0.8	0.4	Increased	Normal	0.4	0.3	0.4	0.3	6,850,000	4,500,000	950	25	8	0	110	98	—	+	5½	17	19	+	

There seems then to be a direct relationship between the fragility of the red blood cells of the new-born infant and the number of immature red cells in the circulation.

Van den Bergh Reaction.—Both qualitative and quantitative van den Bergh reactions were made in thirty-four samples of cord blood. The direct reaction was either negative or greatly delayed. The indirect reaction was positive in every instance. The quantitive test showed a range of from 2½ to 8 units. It is interesting to note that visible icterus developed in all cases in which the van den Bergh reaction showed 4 units or more (table 4).

Icteric Index.—This was done with the peripheral blood of twenty-one infants. It was increased in all instances, the minimum being 7 and the maximum 28 at birth. Icterus was visible in all infants whose icteric index was above 15. In the instances in which icterus developed, the index was higher at the end of ten days than it was at birth. In the few instances in which icterus was not apparent, the indexes fell to nearly normal (5 to 7 units) in about six days. Similar observations were reported by Ada Hirsch [40] with repeated van den Bergh reactions in new-born infants. We preferred the icteric index method, which, while not so exact as the van den Bergh, does not require venipuncture, and for clinical purposes yields as satisfactory results. The technic used was that of Davis.[41]

There is, therefore, a direct relationship between the quantity of bilirubin in the blood as shown by both the van den Bergh and the icteric index and the appearance of icterus; however, we feel that the presence of visible icterus is a matter of degree only and that new-born infants cannot be properly divided into icteric and nonicteric types. Icterus neonatorum may be considered as a physiologic condition present in all new-born infants. The appearance of visible icterus is merely a matter of the degree of hemolysis taking place. The constant presence of an increased indirect van den Bergh reaction, together with the observations of spontaneous hemolysis of cord blood; the increased fragility in cord and peripheral bloods, as well as the return of the fragility to normal with the disappearance of the immature cells of the blood all point conclusively to a hemolytic origin of icterus neonatorum. Theories relating to infection in hepatic disturbances, blocked ducts, etc., most of them being purely empiric, lose all their bases in the face of these facts. It has been shown many times that the infant is born with a polycythemia. Table 4 shows that all of

40. Hirsch, Ada: Ztschr. f. Kinderh. **9**:196, 1913.

41. Davis, D.: Am. J. M. Sc. **172**:848, 1926.

our cases gave a red blood count above 5 million, being usually between 6 and 7 million. The red cell count falls rapidly within the first two or three days, and this fall coincides with appearance of icterus.

SUMMARY OF OBSERVATIONS

1. Umbilical cord blood hemolyzes rapidly on standing in a test tube. This occurs equally when the corpuscles remain intact with the serum and when the serum is replaced by physiologic solution of sodium chloride. Adult blood treated in the same manner does not behave in this way.

2. There is a marked increase in the fragility of red corpuscles of cord blood. The same increase in fragility was found in the peripheral blood of infants. The resistance returns to normal or above normal at the end of about one week.

3. The presence of a hemolysin in the maternal blood against the infant's corpuscles, as claimed by Mitchell, could not be confirmed. No hemolysin could be demonstrated in the infant's serum.

4. An increase in the number of immature red cells, reticulated forms and nucleated red cells was found in the cord blood and in the peripheral blood. The disappearance of these forms from the circulation was found to coincide with the return of the fragility to normal.

5. Studies of unhemolyzed fractions in fragility tests showed that the immature forms were more sensitive to saline dilutions. The reticulated cells disappeared first, and the nucleated red cells second. The immature forms in the circulation disappeared in the same order.

6. An increase of bilrubin was found in the cord serum and peripheral blood of all the infants examined. The van den Bergh test done on cord blood gave an indirect reaction never below 2½ units, and as high as 8 units. The icteric index, done on peripheral blood, showed values from 7 to 28 at birth—it did not return to normal by the end of ten days. In fact in all cases in which visible icterus was present, it was actually increased at the end of this time. In the cases in which the index was 11 or lower at birth, it fell slightly in ten days.

COMMENT

The presence of icterus, to a greater or lesser degree in all newborn infants, and the coincidence of its development with (1) the disappearance of the polycythemia, (2) the gradual disappearance of immature red cells, (3) its association with an increase in the fragility of the red cells and (4) the presence of indirect van den Bergh reactions and a constant increase of the icteric indexes, all amply prove the hemolytic nature of icterus neonatorum. Table 4 shows that polycythemia was present at birth in all of the thirty-nine

infants of this series and that a rapid fall in the red cell count took place within the first twenty-four hours after birth, reaching its maximum within about one week after birth. This phenomenon is well recognized, and we believe it to be intimately associated with the mechanism of icterus. If the explanation for the presence of polycythemia at birth and for its subsequent disappearance can be given, then we shall have adequately explained the phenomenon of icterus neonatorum once it is granted that this condition is entirely hemolytic in origin. Why does the new-born infant have a polycythemia? If one considers the fetal circulation for one moment the question will answer itself. The fetus resembles the person with congenital heart disease. Except for a small portion of the umbilical vein, pure arterial blood does not exist in the circulation. The fetus lives in a constant condition of oxygen want; he is or should be cyanotic. This chronic oxygen want in prenatal life has the same effect that chronic oxygen want would have under any circumstances (congenital heart disease, living at high altitudes), namely, that the bone marrow is stimulated and an increased number of red cells is produced. Very soon after birth a change takes place; anoxemia no longer exists. Except in children with congenital cardiac malformations, there is no longer an admixture of arterial and venous blood. The necessity for polycythemia ceases with the birth of the child, and the excess of red cells is destroyed; hence the icterus. The new-born child comes down, as it were, from a high altitude, and, just as in coming from a high altitude polycythemia and immature forms disappear from the circulation, so the fetus readjusts its blood to the normal oxygen tension under which it lives. Huggett,[42] working with goats, has shown that the oxgen tension of the arterial blood of the fetus is much lower than that of the mother. Our studies of the oxygen tension of the human fetus will appear in a later communication.

CONCLUSIONS

Icterus neonatorum is a physiologic condition which is the result of a postnatal readjustment from an environment requiring the presence of polycythemia for the maintenance of oxygenation to one in which no such extraordinary measures are necessary. Icterus is present in all infants, visibility being only a matter of degree.

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42. Huggett, A. S.: J. Physiol. **62**:373, 1927.

PATHOLOGIC CHANGES IN THE LARGE INTERLOBAR FISSURES IN CHILDREN *

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In a former communication, I [1] suggested a method for the roentgen study of the large interlobar fissures which was cited in the German literature by Holzknecht,[2] later by Eisler [3] and by Wimberger,[4] and which was elaborated in detail by Fleischner.[5] This method is not in common usage, and it is for this reason that cases are presented to illustrate the technic which deserves reintroduction into American usage.

ANATOMY

The Left Interlobar Fissure.—The left interlobar fissure may be represented by a line beginning from 6 to 8 cm. below the apex at about the level of the third dorsal vertebra, extending from the posterior margin of the medial surface of the lung, backward and slightly upward to the posterior surface, then arching slightly over the posterior convexity and downward; it crosses the fourth interspace in the midaxillary line, to the level of the sixth costal cartilage, cutting the lung above the cardiac incisure.

Thus it makes of the inferior part of the lower lobe what was called by Luschka [6] a tongue-shaped process of lung, which is now known as the lingula. This represents the external marking of the left (great) interlobar fissure; the diaphragmatic and mediastinal markings were not portrayed until Fleischner adequately described them. If the line previously described is continued dorsally and medially on the diaphragmatic surface toward the lower medial margin of the lung below the hilum, then extended slightly dorsally, upward to the hilum and from above it steeply to the level of the third dorsal vertebra, the diaphrag-

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* From the Pediatric Service and the Radiological Service, the Mount Sinai Hospital.

1. Stoloff, E. Gordon: Primary Infection in Tuberculosis, Am. J. Dis. Child. **33**:363 (March) 1927.

2. Holzknecht: Die Roentgen Diagnostik der Erkrankungen der Brusteingeweide, Hamburg, 1901.

3. Eisler: Interlobare pleuritische Schwarte der kindlichen Lunge im Roentgenbilde, München. med. Wchnschr. **35**:10, 1912.

4. Wimberger: Personal communication to the author.

5. Fleischner: Lobar und interlobare Lungenprozesse, Fortschr. a. d. Geb. d. Röntgenstrahlen. **30**:185, 1922.

6. Luschka: Anatomie des Menschen, Tubingen, 1863, vol. 1, p. 283

matic and mediastinal markings are obtained. Because of the predominantly left-sided position of the heart, only a narrow part of the upper lobe has a diaphragmatic surface.

The Right Interlobar Fissure.—The right side shows differences from the left. The right interlobar fissure is represented by a line starting at the level of the third dorsal vertebra as the one on the left side does, extending posteriorly to the posterior convexity of the lung, over which it then arches with a convexity even less marked than on the left side, and therefore begins its descent toward the axilla on a less steep incline. The diaphragmatic surface is reached in the anterior or midaxillary lines, or between the two; from there it takes its course on the diaphragm obliquely, posteriorly and medially toward the lower

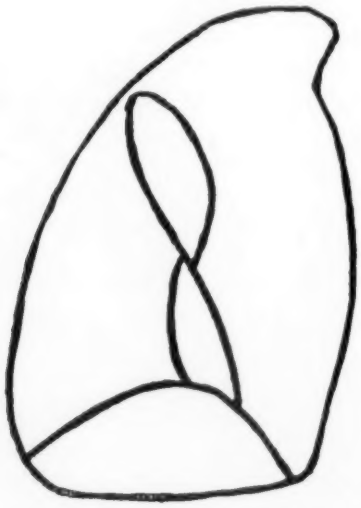

Fig. 1.—The great interlobar fissure (after Dietlen).

part of the hilum, the lung tissue lying anteriorly and medially (middle lobe), thus comprising one-fourth of the diaphragmatic surface. The mediastinal course is similar to that of the left side.

The interlobar fissures are to be thought of as surfaces, and these surfaces are not plane. If the great fissure markings as given are projected on a flat surface, then there will be seen a propellor-like figure, as described by Dietlen,[7] or a "figure 8" (fig. 1). The figure on the left side has longer and narrower loops.

These fissures may be visualized as oval surfaces which, lying at an angle of 45 degrees with the bases of the lung, have been twisted

7. Dietlen: Ueber interlobare Pleuritis, Ergebn. d. inn. Med. u. Kinderh. **12**:196, 1913.

on themselves with the level of the hilum as the fulcrum, so that the upper half faces forward slightly laterally, and the lower half faces forward and somewhat medially.

Because the fissures vary in their depth, complete separation into lobes is variable; there may be only a pleural bridge connecting two adjacent lobes, or only a small pulmonary pedicle; two lobes may be continuous one with the other, so that only a small superficial separation occurs. This is of importance when interlobar pathologic changes are considered.

The pleurae should be thought of as a serous membranous sac, which is so invaginated at the hilum by the lung that the costal diaphragmatic and the interlobar mediastinal surfaces, except in the area in which the vessels and bronchi enter, are completely covered by a serous membrane, so that each of these surfaces has two adjacent layers of pleurae.

PATHOGENESIS

The pleural coverings of the fissures may become involved secondary to pneumonia, rheumatic cardiac disease, tumors in the thorax and tuberculosis. In the last mentioned condition, because the primary focus usually lies subpleurally, it causes a concomitant involvement of the pleurae. This may manifest itself as an adhesive pleuritis close to the site which shows a traction toward the infection. The pleuritis may be limited to this area or may extend over the entire surface of the lung. The reaction may be fibrinous, serous, hemorrhagic or a combination of these types. The dry fibrin with a little serous exudation is productive of fibrous tissue of varying density and extent. Exudation is of varying intensity. Healing occurs with localized or extensive adhesions; the process, however, may be so widespread as to lead to synechiae of the pleurae. If a caseous focus perforates the pleural cavity, a caseous pleuritis will result; in such instances, healing may be accompanied by calcification and even by ossification. The condition usually found is a localized fibrinous pleurisy. Because of their location near the pleurae and frequently within the fissures, the lymph glands like the primary focus may cause pleurisy of the mediastinum and interlobar fissures.

TECHNIC

For a roentgen diagnosis of interlobar pathologic changes, it is indispensable to perform a fluoroscopic examination which permits a study of the respiratory movements in varying positions which is not permitted by roentgenography alone. A consideration of the structure of the fissures as previously described indicates that the small fissure between the right upper and the middle lobes permits a visualization of any pathologic change in the usual postero-anterior position, since the fissure lies practically horizontal to the central beam of the tube

and, too, of the azygos fissure (that fissure which separates the azygos lobe from the rest of the right upper lobe). The great interlobar fissures, in the usual postero-anterior position, may fail to reveal interlobar disease unless it is extensive. The central beam in this instance passes through the fissure. If, however, the fissure is rotated on its axis so that the central beam passes through the entire length of the fissure, an impression of any pathologic condition present, even if it is of limited extent, is made on the roentgenogram. The rotation of this axis may be accomplished in one of two ways. A lordotic position is achieved simply by telling the patient to hold his shoulders back and to stick his abdomen forward as far as possible. The tube is then put behind the patient at about the level of the fourth or fifth dorsal spine, and the plate is placed opposite the same point. If, however, cooperation cannot be obtained, if the child is too young and unintelligent, or if he moves, the same result can be achieved by placing the tube at about the level of the first or second dorsal vertebrae and the plate relatively low, for the impression in this case is cast low on the plate. A lateral position is also of great assistance when high voltage is used, so that any possible pathologic change in the fissure may be seen through the shadow of the heart.

DIAGNOSIS

Not infrequently, there is a haziness of the lung field in the region of the hilum, the nature of which does not become clear until examinations in the lateral and lordotic positions are utilized. The lateral examination will then reveal an oblique shadow included within the density of the heart shadow which is sharply defined and the shape of which will vary with the extent and location of the interlobar pathologic process. It courses downward and anteriorly from the upper and posterior part of the lung. It may be stringlike, bandlike or spindlelike; it may be short or long, depending on the extent and position of the pathologic process. The examination in the lordotic position will show a triangular shadow, its base continuous with the heart and extending into the lung field. The extent and relative proportion of this pennant-like shadow depends on the amount of induration or effusion present, so that the apex of the triangle may have an angle varying up to 90 degrees. During a fluoroscopy these shadows can be made to appear and reappear and to vary from a haziness to a definitely circumscribed triangle by changing the patient from the erect position to the lordotic position or by moving the tube up high and the screen down low, and by lateral examination.

REPORT OF CASES

CASE 1.—C. B., a boy, aged 2 years, was admitted to the Children's Service at the Mount Sinai Hospital, March 17, 1928, with a complaint of a cough of five weeks' duration. There was no history of exposure to tuberculosis. Devel-

opment was normal. Since the age of 10 months, he had had frequent colds. A cough was present, with which a slight fever and occasional croup were associated. For the past five weeks he had had a cough, mostly at night. There has been no production of sputum. Occasional fever was present, but the temperature was not taken. No other symptoms were associated with it.

On physical examination, the boy was pale but did not look ill. His tonsils were large and cryptic. The postcervical glands were hard, discrete and shotty. Those in the left axilla were also enlarged. There was a slight dulness at the base of the right lung; otherwise, nothing abnormal was noted. The abdomen and genitalia were normal. Examinations of the blood and urine showed no abnormalities. The temperature on admission was 99.5 F. and within the next week varied between that and 100.5 F., with an elevation usually in the afternoon and evenings. After a week, it remained normal. The Pirquet examination was negative, but the intracutaneous test of Mantoux performed with 1 mg. of tuberculin gave a markedly positive reaction.

Roentgen examination in the usual postero-anterior positions revealed a faint irregular shadow at the base of the right lung in the cardiophrenic angle which had the appearance of an infiltration. There were irregular shadows at both hila which had the appearance of diseased lymph glands. Fluoroscopy performed with the patient in the lordotic position already described and a roentgenogram made in this fashion revealed a dense, sharply circumscribed triangular shadow, the base of which was continuous with the heart shadow, its apex protruding into the right lung field in the region of the fifth and sixth interspace. This appearance was caused by effusion or a marked pleural thickening in the lower part of the right large interlobar fissure.

In view of the fact that the child was 2 years old and that the tuberculin reaction was markedly positive, the interlobar pathologic change was probably due to tuberculous disease of the tracheobronchial lymph glands and the lymph glands near the large interlobar fissure which had caused an associated pleuritis of the large interlobar fissure.

Lateral examination showed a dense, bandlike shadow coursing obliquely downward and anteriorly overlying the cardiac shadow which corresponded in position to that of the large interlobar fissure on the right side.

Case 2.—H. E., a boy, aged 11 years, had normal family and developmental histories. The past history may be summarized as follows: The boy had bronchitis during his first year. At 2½ years, a tonsillectomy was done. Six months later fever was present, and a physician who was summoned diagnosed rheumatic cardiac disease. When 4 years old, the boy had measles. The next year the patient suffered from scarlet fever, complicated by bilateral otitic disease for which a double mastoidectomy was performed. His stay in the hospital lasted six months. Skin grafts were done on the mastoid. When he was 10 years old, he was kept in bed for a week because of a recurrence of the heart disease and a swelling of the liver. He spent three months at a home for patients with cardiac disease. The present illness began one day after his discharge therefrom, three weeks before admission to Mount Sinai Hospital. On the day following his return home, he had a cough and fever, which lasted until five days later, when he was admitted to the children's service at the Mount Sinai Hospital.

On physical examination, the boy appeared acutely ill and was coughing. Both ears were discharging profusely. The heart showed a systolic murmur which obliterated the first sound and which was transmitted to the axilla. The second heart sound was clear and strong. There was cardiac pulsation in the upper epigastrium. The spleen was palpable; otherwise, there were no abnormalities.

Fig. 2 (case 1).—An irregular shadow at the base of the right lung in the region of the cardiac phrenic angle.

Fig. 3 (case 1).—The same patient in the lordotic position. There is now seen a triangular pennant-like shadow in the region of the right large interlobar fissure.

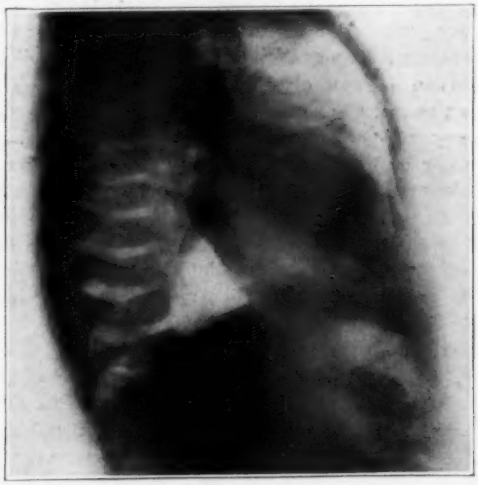

Fig. 4 (case 1).—Lateral view, showing a bandlike shadow in the region of the right large interlobar fissure.

The temperature on the first day of admission was 104 and gradually declined to 100 F., at which it persisted for two weeks and then became normal. The tuberculin reactions (Pirquet and Mantoux, 1 mg.) were negative. Roentgen examination showed a moderate enlargement of the left ventricle and a distinct bulging in the

Fig. 5 (case 2).—A faint shadow fading off into the lung field adjacent to the heart near the base of the right lung.

Fig. 6 (case 2).—Lordotic position, showing a sharply circumscribed triangular pennant-like shadow projecting into the lung field with the cardiac shadow as a base and representing disease in the large interlobar fissure of the right side.

region of the pulmonary artery and the left auricle. The roentgen appearance was that presented by combined mitral disease, although congenital defects could not be excluded roentgenologically. At the right side, adjacent to the heart and continuous with the hilum shadow, there was a faint shadow, fading gradually into the lung, the nature of which was not clear, although it might possibly have

been due to an infiltration. In the lordotic position, however, a dense triangular shadow protruded from the cardiac shadow into the lung field in the region of the sixth interspace, so that it had the appearance of a pennant extending from the mediastinum into the lung field. This was due to a small effusion in the interlobar pleura of the large fissure. A lateral examination showed a spindle-shaped shadow, overlying and parallel to the seventh and eighth ribs in the antero-inferior position of the large fissure. This effusion was probably pleuro-pericardial and associated with the cardiac disease.

SUMMARY

1. Physical examination of the lungs usually fails to elicit evidence of small effusions or limited thickenings of the large interlobar fissures.

Fig. 7 (case 2).—Lateral examination of the same patient. A spindle-shaped shadow lies within the area of density cast by the heart and represents pathologic changes in the antero-inferior position of the large interlobar fissure of the right side.

Roentgen examination in the routine postero-anterior position also fails definitely to reveal such pathologic changes.

2. A technic is again described in which the lordotic position is used in fluoroscopy and film taking and which permits registration of disease of the large interlobar fissures.

3. The lateral position is also helpful and should be used together with the lordotic position in cases of suspected or evident interlobar disease.

4. A case of interlobar pleurisy of the large fissure associated with cardiac disease is presented, and another of interlobar pleurisy of the large fissure associated with disease of the tuberculous lymph glands, both illustrating the sparsity of physical signs and the absence of roentgen evidence when the routine postero-anterior positions are utilized. When the children are examined in the lordotic and also in the lateral positions, the presence and extent of the interlobar pathologic changes become unequivocally evident.

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THE UNUSUAL ASSOCIATION OF POSTINFANTILE RICKETS WITH OSTEOMALACIA *

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In spite of the vast amount of literature recently devoted to different phases of the general subject of rickets, comparatively little attention has been paid to the age limit of its active manifestations. In the main, writers have confined their descriptions of rickets occurring in older children to the occasional picture of "late rickets," and not infrequently differentiation between late rickets and osteomalacia has been so imperfect as to leave the identity of a given case in doubt. Preliminary to any addition to the clinical data existing, a brief citation of representative expressions concerning rickets and osteomalacia is therefore expedient.

MacCallom [1] stated that rickets usually begins at the sixth month, lasting sometimes for several years with remissions and final healing. Delafield and Prudden [2] noted that the disease usually occurs in the first two years of life but may be seen as late as the twentieth year. Hess [3] remarked the commonness of late rickets in the Central Empires during the World War, placing the period of greatest incidence between 14 and 17 years and citing the marked increase of both rickets and osteomalacia throughout the period of the war as evidence in favor of a common etiology.

Still [4] stated that rickets is seldom seen in active progress after the age of 3 years, and that late rickets, while occurring most often between the ages of 9 and 14 years, has actually begun as late as at the age of 17 years. Noting that if the condition begins or recrudescence

* Submitted for publication, Feb. 8, 1929.

* From the Department of Diseases of Children, Columbia University College of Physicians and Surgeons.

1. MacCallom: American Text Book of Pathology, Philadelphia, W. B. Saunders Company, 1928, p. 919.

2. Delafield and Prudden: Text Book of Pathology, revised by Wood, New York, William Wood & Company, ed. 14, 1927, p. 1072.

3. Hess, in Abt, I. A.: Pediatrics, Philadelphia, W. B. Saunders Company, 1923, vol. 2, p. 911.

4. Still, in Osler and McCrae: Modern Medicine, Philadelphia, Lea & Febiger, 1925, vol. 2, p. 847.

occurs after 4 years of age the disease might properly be described as late rickets, this observer cited an active case in a boy, aged 9½ years, in whom the disease had been almost quiescent during a long interval following the patient's earliest years.

Baetjer and Waters [5] described rickets as occurring before the age of 3 years. Holmes and Ruggles [6] characterized the changes as belonging to the first period of dentition, with frequent occurrence in the second and third years. These authorities also mentioned rickets of adolescence, which is characterized by irregular rarefaction and enlargement of the long bones resulting in disturbance of the weight-bearing function associated with deformities such as genu varum and coxa vara.

Bythell and Barclay [7] of London stated that rickets is of frequent occurrence in children, chiefly in the second and third years. Schanz [8] stated that rickets is limited to the second, third and fourth years. Gleich [9] reported a case of "inveterate rickets" in a colored boy of 4 years who was underweight and presented typical signs and symptoms of extensive rickets, both healed and active.

The citations which have been made might readily be supplemented at length if they were not sufficiently representative of the present knowledge. Comby's [10] statistics are both comprehensive and illustrative: 1,268 of 1,662 patients with rickets were between 1 and 2 years of age.

Osteomalacia, which closely simulates late rickets and is considered by many to be practically identical with rickets, occurs typically in persons whose endochondral ossification is complete, particularly in women, with exacerbations during pregnancy and the nursing period. In this condition, softening of the bone occurs by halisteresis or removal of inorganic salts. Associated parathyroid lesions in the subjects, which are accountable for deficiency of calcium, have been reported. In Vienna, particularly during the years 1918-1920, hunger osteomalacia, frequently observed in conjunction with tetany, affected elderly persons of both sexes. Although these patients invariably responded to full doses of cod liver oil [11] and despite Miles' and Feng's

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5. Baetjer and Waters: Injuries and Diseases of the Bones and Joints, New York, Paul B. Hoeber, 1921, p. 188.

6. Holmes and Ruggles: Roentgen Interpretation, Lea & Febiger, 1921, p. 80.

7. Bythell and Barclay: X-Ray Diagnosis and Treatment, Oxford Medical Publications, 1912, p. 38.

8. Schanz: Praktische Orthopaedie, Berlin, Julius Springer, 1928, p. 560.

9. Gleich: Arch. Pediat. **45**:504 (Aug.) 1928.

10. Comby, in Osler and McCrae: Modern Medicine, Philadelphia, Lea & Febiger, 1925, vol. 2, p. 380.

11. Great Britain Med. Research Council, Special Report Series, 1923, no. 77, p. 191.

claim that persons with osteomalacia can be cured with a fat soluble vitamin,[12] MacCallom [1] did not confirm this specific action.

Diven [13] stated that osteomalacia of infancy appears about the time the child begins to walk, or a little later. According to this authority, at times a similar condition has followed an infectious disease.

Jones and Lovett [14] recorded that true idiopathic osteomalacia in a serious form occurs occasionally in children and is distinct from rickets in the absence of epiphyseal changes characteristic of the latter disease.

Hutchinson and Stapleton [15] saw no justification for the separation between rickets and osteomalacia and stated that the conditions are the same and represent rickets at different ages.

Stapleton [16] reported intermediate stages showing characteristics of both rickets and osteomalacia, depending on the age of the patient.

Holmes and Ruggles [6] classified the bony lesion of osteomalacia under the main division of "Generalized and Rare Diseases." Bythell and Barclay [7] raised the question whether osteomalacia really occurs in childhood. Baetjer and Waters [5] held that the disease belongs to the third age period, from 40 years on.

Other evidence confirms the report of Schanz,[8] who divided these lesions into three groups comprising late rickets, hungerosteopathy and hungerosteomalacia. Schanz held the view that if these three disease processes are essentially the same as rickets or occur as closely related conditions, the eventual differentiation must be made by the pathologist or anatomist.

Dwyer and Ekelberry [17] presented a careful review of the subject of osteomalacia in children and reported the cases of a girl of 5 years and a boy of 12 years. Studies on the mineral metabolism in these cases showed lowered retention of calcium, phosphorus and magnesium. Miles and Feng [12] similarly found a negative calcium balance in three of four cases of osteomalacia.

After reviewing the literature, Dwyer and Ekelberry endorsed Cohnheim's view that rickets is characterized by a faulty deposition of mineral matter in young bone that has not yet undergone ossification,

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12. Miles and Feng: J. Exper. Med. **41**:137, 1925.

13. Diven, in Abt, I. A.: Pediatrics, Philadelphia, W. B. Saunders Company, 1923, vol. 2, p. 253.

14. Jones and Lovett: Orthopedic Surgery, New York, William Wood & Company, 1923, p. 389.

15. Hutchinson and Stapleton: Brit. J. Child. Dis. **21**:96, 1924.

16. Stapleton: Lancet **1**:1119, 1925.

17. Dwyer, H. S., and Ekelberry, O. S.: Osteomalacia in Children, Am. J. Dis. Child. **31**:639 (May) 1926.

while the essential process in osteomalacia is substitution of organic matter for mineral matter in bone that is mature. Rickets, according to this belief, thus typically affects the epiphyses in developing bone; osteomalacia, the interior of fully formed bone.

In marked cases of osteomalacia, replacement of the bony tissue within the medullary spaces by soft and friable osteoid tissue lacking in lime salts gives rise to a cystic appearance in the x-ray picture of the long bones. Although the existence of osteomalacia in childhood has been questioned and its occurrence, if it does occur in children, must be rare, the roentgen appearance in the bones of the children whose cases are here considered as those of osteomalacia is certainly much the same as that of the bones of adults with osteomalacia (figs. 4 and 5).

The following case reports from the 1928 summer service of the Seaside Hospital of St. John's Guild, New York, illustrate the fallaciousness of the popular belief that active rickets is a disease limited to the first two or three years of life. The reports further emphasize the extreme importance of careful routine roentgen studies in rachitic cases before the institution of operative orthopedic measures, in order that the surgeon may be sure that the structures on which he works will not be subject to recurrence of static insufficiency and deformity. Correlation of our observations with the rather meager reports available concerning osteomalacia warrants the belief that osteomalacia is of more frequent occurrence and of more grave significance than has been generally believed, since, notwithstanding the fact that this disease is usually recognized only after advanced changes have occurred, slight forms recognizable as soon as static insufficiency is noticed are incomparably more frequent, the osteomalacia insufficiencies being rather numerous. Certainly the possible existence in advanced cases presenting "rachitic deformity," of actual osteomalacia masked by the primary associated rickets, opens up a field of great importance, especially to the orthopedist.

REPORT OF CASES

CASES 1, 2, 3 and 4.—Mary, Evelyn, Olga and Eileen H., colored sisters, aged 2¼, 3½, 4⅚ and 6 years, respectively, were admitted to the Seaside Hospital, June 11, 1928, with advanced rickets complicated by extreme deformities calling for operative orthopedic treatment.

The family history was negative for both syphilis and tuberculosis. Four other children, one of whom was the youngest member of the family, were at home and were in fair health. Prior to the birth of Eileen, aged 6 years, the mother had had two miscarriages, the first at the end of the second month, the second at the sixth week of pregnancy. All of the patients were born normally at term without instrumental aid and without subsequent convulsions, and all were breast fed in part for from six to eight months. Grade B milk, boiled with barley water, sup-

plemented the breast milk after the third month. During infancy, all the children received orange juice, spinach and mashed potato. Egg and meat were given rarely in the period directly following infancy. Eileen received no cod liver oil till she was 4 years of age. At this time both she and her sisters were given the oil in amounts ranging from 3 to 4 teaspoonfuls as the individual daily dosage. Presumably Mary, the youngest, received the oil earlier in life than the other children, although the record on this point is not dependable.

None of the four patients had a record of serious past illness.

It is noteworthy that the family lived on the ground floor for three years without sunshine, and that except for occasional afternoon trips to a nearby park the children were all kept indoors.

A fair conception of the physical condition of the four may be gained from figure 1. All showed pronounced rachitic deformities so serious as to constitute actual crippling. Mary, aged 2¼ years, could not walk and Eileen, according to

Fig. 1 (cases 1, 2, 3 and 4).—Appearance of Mary, Olga, Eileen and Evelyn H., aged 2¼, 4⅝, 6 and 3½ years, respectively.

the mother, had not walked until she was almost 4 years old. All four patients were markedly under the normal standards for weight and height. Intradermal tuberculin tests applied to the three older children were negative. During their stay in the hospital, they underwent tonsillectomy without difficulty. With the exception of the evidences of rickets afforded by physical examination and the x-rays, none of the children presented any signs of constitutional disease. Wassermann tests of the blood performed on Olga and Eileen were negative. During the period from June 11 to August 27, the date of discharge, Mary gained 3½ pounds (1.6 Kg.); Evelyn, 2¼ pounds (1 Kg.); Olga, ¾ pound (0.3 Kg.) and Eileen, 1 pound (0.5 Kg.). How far below the normal was the nutrition of each child even after approximately two and a half months of hospital care is apparent from the following tabulation of their weight: Mary, 2½ years, 22½ pounds (10.2 Kg.); Evelyn, 3½ years, 25¾ pounds (11.6); Olga, 5 years, 27 pounds (12.2 Kg.); Eileen, 6 years, 30½ pounds (13.8 Kg.).

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Fig. 2 (case 1).—The characteristics of ordinary rickets in the long bones are apparent in this child.

Figures 2, 3, 4 and 5 present evidence of unusual changes in the bones to which further reference must be made, and at the same time show a definite improvement in keeping with the clinical observations.

Treatment was not selective, but included sunlight treatment on the beach, Alpine lamp treatment indoors and administration of cod liver oil, with the general aim of curing rickets, irrespective of the aid employed, without unnecessary delay.

Because of the evidences afforded by the x-rays of active lesions of the bones, it was necessary to postpone the operative treatment which the bowleg and knock-knee deformities will eventually require.

Fig. 3 (case 2).—The characteristics of ordinary rickets in the long bones are apparent in this child as well as in her sister (fig. 2).

Case 5.—Wilfred H., a colored boy, aged 3 years and 9 months, was admitted to the Seaside Hospital, July 16, 1928, for the treatment of active rickets and gingivitis. The family history had no bearing on the patient's condition. He was born normally, weighing 7½ pounds (3,401.9 Gm.), nursed for six months and was then given modified milk. Details concerning his subsequent diet are lacking, and it is doubtful whether he received cod liver oil during his infancy. A few weeks or months prior to admission, he had measles.

On physical examination the child appeared poorly nourished, poorly developed and rachitic; he weighed 26 pounds (11.8 Kg.). A flaring costal arch, beaded

Fig. 4 (case 3).—In addition to the typical rachitic changes as shown in figures 2 and 3, there is apparent in the bones depicted in this figure a superimposed condition of osteoporosis, the changes in the epiphysis and shaft together affording an appearance more complex than that found in the typical picture of osteomalacia lesions in adult bones. *C* was taken six weeks later than *A* and *B* and shows marked improvement with epiphyseal restoration and slight increase in the density of the shaft.

Fig. 5 (case 4).—The changes noted in figure 4 are observed in greater degree here, evidence of osteomalacia in the bones of this 6 year old subject being, if anything, more marked than in those of her next younger sister. The epiphyseal picture is that of the so-called florid rickets, observable not only at the wrists and ankles but also at the knees and elbows. Rarefaction in the diaphysis has progressed to a stage too advanced to be explained by infantile rickets of the ordinary type and from the roentgen standpoint justifies the use of the term osteomalacia. Improvement after six weeks' treatment (*C*) is apparent as in the case of the younger sister (4 *C*).

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Fig. 6 (case 5).—The association of osteomalacia-like lesions with active rickets as shown in figures 4 and 5 is exemplified in the case of an unrelated boy. *A* and *B* were made on admission; *C*, after a little more than a month of hospital care.

ribs, distended abdomen, enlarged epiphyses and marked anterior bowing of the tibiae and radii were present. First dentition was complete, but the teeth were carious, the gums were acutely inflamed and the tonsils were enlarged, injected and cryptic. Intradermal tuberculin and blood Wassermann tests were negative. With improvement in the stomatitis, the patient's temperature, which reached 101.5 F. shortly after admission, fell to normal on the fourth day, and he made favorable progress during the remainder of his stay of approximately six weeks in the hospital, gaining 2½ pounds (1.1 Kg.) and undergoing a successful tonsillectomy combined with extraction of eight carious teeth. Treatment consisted in heliotherapy and administration of cod liver oil.

In this case, as in cases 3 and 4, the evidence afforded by the x-ray (fig. 6) was such as to preclude the possibility of early orthopedic operative treatment and suggests most strongly the presence of true osteomalacia.

Films of the chest in all the cases cited showed nothing unusual, with the exception of the ordinary signs characteristic of rickets, particularly the rosary and the rachitic involvement of the proximal end of the humerus.

CONCLUSIONS

1. Active rickets is by no means uncommon in early childhood after the age of 3 years and before adolescence.

2. Although osteomalacia has not been considered a disease of childhood, the existence of defects of the bone characteristic of this condition has been shown in three patients of our series ranging in age from 3½ to 6 years.

3. Although rickets and osteomalacia have not been proved essentially identical, the observations recorded suggest that there may be no definite dividing line between the two conditions.

4. In three of the cases presented, the coexistence of postinfantile rickets and osteomalacia seems beyond question, notwithstanding the admitted infrequency of such association.

5. Recognition of postinfantile rickets and of osteomalacia, whether occurring singly or combined or as separate phases of an identical disease process, is of the utmost importance to the orthopedic surgeon, since no operation should be performed on patients in the active stage of rickets or osteomalacia.

Case Reports

A TRACHEAL FOREIGN BODY SIMULATING DIPHTHERIA *

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I am reporting this case of foreign body in the trachea to point out the importance of accurate and careful history-taking in children in whom laryngeal symptoms suddenly develop and persist in spite of ordinary methods of treatment. I am reporting it also to show the value of more than one laryngoscopic examination in those cases in which a diagnosis of laryngeal diphtheria might be doubtful, especially with a history of circumstances under which a foreign body might have been aspirated.

REPORT OF CASE

On Nov. 1, 1923, M. F. R., a girl, aged 4 years, developed a cold, with sneezing, running eyes and cough. Her appetite was good, however, and at supper she was given the "bone of a potroasted lamb." While eating the meat from the bone she suddenly screamed, began to choke and then lost speech completely. She was immediately taken to a physician's office, where the foregoing history was given. The condition was tentatively diagnosed as laryngeal diphtheria, but the mother was told that in view of the fact that possibly a piece of bone had been aspirated, the child should be taken to a hospital for further examination. At the hospital a provisional diagnosis of "laryngitis" was made, and the mother was advised to take the infant to the ward for a few days' observation. She thought that she might have been mistaken regarding the bone, since no bone had been discovered, and accordingly took the child home, where the family physician administered 10,000 units of diphtheria antitoxin. During this procedure, the child regained her speech momentarily "from fright." She did not sleep during the night because of laryngeal stridor, which was found to be less alarming when the head was held over the mother's shoulder. When the child was in a recumbent position, the stridor and dyspnea immediately increased. At 10 o'clock the next morning the child was sent to a hospital for contagious diseases, with a diagnosis of laryngeal diphtheria. Laryngoscopic examination was done, but there was so much swelling of the arytenoids and surrounding structures with such a large amount of secretion that no foreign body was seen. The condition was thought to be diphtheria. In the hospital the child improved; therefore intubation, which had been suggested, was not done. An x-ray picture was to have been taken, but this was not done. On Nov. 17, 1923, the child was discharged from the hospital.

On her return home her breathing was "bad," and she had a cough which was "due to bronchitis." This bronchitis persisted in spite of medication for the rest of the winter, the breathing always being "very heavy" with a "wheezing in the

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* From the Oto-Rhino-Laryngological Service of Bellevue Hospital.

chest." When excited, or after being disciplined, she invariably "choked up," became blue, and had so much dyspnea that the family physician was often called. When he arrived, the attack had usually subsided. Similar symptoms often occurred while the child was eating, and every night since the first symptoms appeared (Nov. 1, 1923) she had awakened two or three times because of shortness of breath.

On Jan. 31, 1925, the child was cross, and the father attempted to discipline her. She began to cough, and shortly after brought up a considerable amount of mucus. Later, while she was eating bread and butter, there was a violent coughing spell which could not be alleviated. No diagnosis was made at that time, but diphtheria was suspected. No antitoxin was given, and there was no improvement in the child's condition. Dyspnea became more marked, and the child became weaker. She refused to eat and apparently had fever.

On February 12, the attending physician told the mother that "there was no sign of diphtheria, nor pneumonia, and there was no temperature." He thought that the condition was spasmodic croup or was caused by a piece of bread aspirated during the choking spell of January 31.

The following day the patient was still worse, breathing rapidly, with marked stridor. There was a "gurgling in the throat that sounded like a death rattle," and the child could not lie down without the most alarming distress. She had slept the preceding night on her elbows and knees, with the head hanging down, awakening every three or four minutes.

The physician advised hospitalization and endoscopic examination to determine whether a foreign body was present in the larynx or tracheobronchial tree. When the child was brought to the hospital, the admitting physician so strongly suspected laryngeal diphtheria that admission to the otolaryngologic service was made only after considerable delay.

On direct laryngoscopy a black object, lying anteroposteriorly across the glottic chink, was seen about 2.5 cm. below the cords, completely shutting off the view into the trachea. This object was pushed with laryngeal grasping forceps so that it lay flat on the posterior wall of the trachea where it was grasped and removed through the laryngoscope.

After the removal of the foreign body, which turned out to be a piece of bone, there was an immediate partial relief from symptoms. There was less stridor; the pallor disappeared, and the mucous membranes became normal in color. Tracheotomy was unnecessary. The temperature dropped from 100.2 to normal during the next twelve hours, and the patient was allowed to go home.

The piece of bone was 1.5 cm. long and 0.75 cm. wide at the widest end, tapering to a point. It was the thickness of a piece of cardboard at the wide end and of tissue paper at the pointed end.

One year later, the patient was in perfect health. She had had no symptoms since the piece of bone was removed from the trachea.

In this case there was found in the trachea a foreign body that was freely movable at the point from which it was extracted, and about which there was no visible pathologic process. It seems likely that it traveled up and down the trachea, influenced by gravity, the respiratory movements and the air currents, and caused severe symptoms only when its position was such that it offered an obstruction to the passage of air.

ENCEPHALITIS ACCOMPANYING WHOOPING COUGH

CLINICAL HISTORY AND REPORT OF POSTMORTEM EXAMINATION *

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AND
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The cerebral complications of whooping cough have been attributed to many causes, among which toxemia, hemorrhage, encephalitis, meningitis and tetany are most frequently cited. Reports of pathologic examinations supporting diagnoses of toxemia or hemorrhage or meningitis have been made, but descriptions of an accompanying encephalitis are rare, although much clinical evidence exists to suggest that this condition is present in certain patients. A review of the American literature reveals no pathologic report of this type of encephalitis.

Hada,[1] in writing of the meningeal complications of whooping cough in 1913, described "acute encephalitic changes in parts of the brain adjacent to a profuse exudate in the sulci." Attention was called in this paper to the similarity of pertussis encephalitis and encephalitis complicating influenza. The same author emphasized the fact that until 1913 no case had been reported in the literature of an isolated cerebral hemorrhage in whooping cough, which was not associated with a hemorrhagic encephalitis or a meningitis.

In 1924, Husler and Spatz [2] described "a typical regressive transformation in the nerve cells of the cerebral cortex in pertussis encephalitis which consisted of a loss of the staining properties of the cells with an obliteration of the Nissl picture; the nucleus alone remained. Certain vacuoles, particularly in the hippocampus major area, were considered to be the sites of completely degenerated ganglion cells." The authors were inclined to view these changes as resulting from other than inflammatory processes. One year later, Jochims [3] was able to confirm

* Submitted for publication, Feb. 22, 1929.

* From the Departments of Pediatrics and Pathology, New Haven Hospital and Yale University School of Medicine.

1. Hada, B.: Ueber die Gehirncomplikationen des Keuchhustens mit besonderer Berücksichtigung der Pachymeningitis productiva interna, Virchows Arch. f. path. Anat. **214**:206, 1913.

2. Husler, J., and Spatz, H.: Die Keuchhusten-Eklampsie, Ztschr. f. Kinderh. **38**:428, 1924.

3. Jochims, J.: Ein Beitrag zur Keuchhusten-Encephalopathie, Ztschr. f. Kinderh. **45**:326, ~~1925~~ 1927.

the histologic alterations described by Husler and Spatz in a patient who came to autopsy; he stressed particularly the fat-bearing glial cells in the hippocampus. Although agreeing with the previous authors that no evidence of edema, exudate, hemorrhage or necrosis was present in the brains examined, Jochims deemed it probable that the changes described were produced by an earlier inflammatory process.

Berardi [4] (in two patients) and Blasi [5] (in one patient) have recently mentioned encephalitis as a cerebral complication of pertussis, but all three children with the disease recovered. Similar clinical reports without postmortem examinations are numerous in the literature.

In view of the paucity of anatomic proof to substantiate the diagnoses of encephalitis in cases of whooping cough showing cerebral signs, the following report is presented. At postmortem examination, the patient was shown to have an acute diffuse encephalitis; the finding of a subarachnoid hemorrhage adds to the interest of the case.

REPORT OF CASE

History.—P. P., a white girl, aged 4 months, was admitted to the wards of the New Haven Hospital on Feb. 28, 1928, with a complaint of convulsions of four days' duration. The family history revealed that the mother had had eight pregnancies; the patient was the last child; there had been no miscarriages or premature labor. The second child died of "summer complaint" when 3½ months old. All the other children were well at the time this patient was admitted to the hospital, but all had had whooping cough at some time just previous to the onset of this child's illness.

The patient was born at full term and weighed 6 pounds and 9 ounces (2,982.7 Gm.) at birth. The labor was reported as spontaneous. Jaundice soon after birth was the only unusual occurrence during the neonatal period. The child was artificially fed with a diluted formula of whole milk-water and dextrimaltose. Cod liver oil or orange juice had not been given.

The present illness began with cough, approximately four weeks prior to admission to the hospital. The cough was diagnosed as pertussis; it was severe and accompanied by much vomiting, but there was no history of bleeding from the nose or into the conjunctivae. The child was under the care of a physician and was apparently progressing satisfactorily until four days before admission when, at 4:30 in the morning, she had her first convulsion. As described, this was tonic and clonic in type and precipitated a severe coughing attack which lasted fifteen minutes. She had six other convulsions that day with much vomiting and some fever. There was no history of an inspiratory crow or the holding of the hands and feet in a position characteristic of tetany. The child was free from convulsions during the two following days, but on the morning of the fourth, convulsions were so frequent that the mother could not keep count of the number; hospitalization was advised.

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4. Berardi, A.: Contributo clinico allo studio delle complicanze cerebrali da pertosse, Pediatria **35**:188, 1927.

5. Blasi, G.: Un caso di complicanza cerebrale da pertosse con esito in guarigione, Policlinico (sez. prat.) **34**:1580, 1927.

At the time of admission, the child was poorly nourished, desperately ill and in a state of continuous convulsion. The temperature was 40.8 C. (105.4 F.). Respirations were irregular in rhythm and character. Definite pallor and slight cyanosis were present. The convulsions were of the nature just described and involved the whole body. No general glandular enlargement existed. Examination of the head showed a soft, flat, nonbulging anterior fontanel, continued nystagmus, reddened ear drums, a moderate nasal discharge and an inflamed pharynx. The neck was not stiff. The heart was not enlarged; the rate was rapid. No murmurs were heard. The lungs were resonant; there were no changes in the breath sounds, but a few subcrepitant râles were heard over the left interscapular area. The liver was palpable 1½ fingerbreadths below the costal margin.

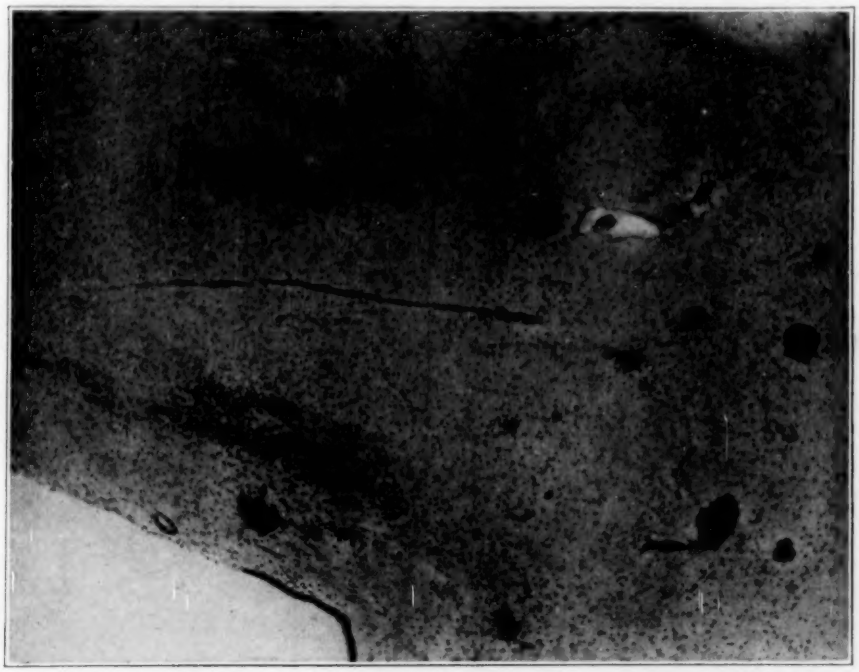

Fig. 1.—Mononuclear cellular infiltration in the hippocampus. Hematoxylin and eosin stain; × 70.

The child was given a few whiffs of ether. After a few inhalations, she became apneic; caffeine was given hypodermically, and the child was placed in a mustard bath. The respirations improved somewhat in quality. Intravenous injections of dextrose were administered, but convulsions occurred more or less continuously. Blood was taken for determinations of calcium and phosphorus[6] which were reported as 8.98 and 7.3 mg. per hundred cubic centimeters of serum, respectively. Following the continuous observation of the child for about five hours, it was noted that she had a left internal strabismus and clonic contractions of

6. These determinations were made because Powers (Tetany as a Cause of Convulsions in Whooping Cough, Am. J. Dis. Child. **30**:632 [Nov.] 1925) found hypocalcemia in certain patients with convulsions complicating whooping cough.

the left arm. Breathing became more difficult and irregular; convulsions continued, and the child died, apparently of respiratory failure, seven hours after admission. A blood culture obtained immediately after death was sterile. Spinal fluid obtained soon after death was sterile but bloody.

The postmortem examination was performed three hours after death; the positive observations only are recorded here.

The body of the infant was pale and puny, weighing 3,500 Gm. There was no discharge from any of the body orifices. The conjunctivae were pale and clear; the pupils were equal and regular, each measuring 3 mm. in diameter. The

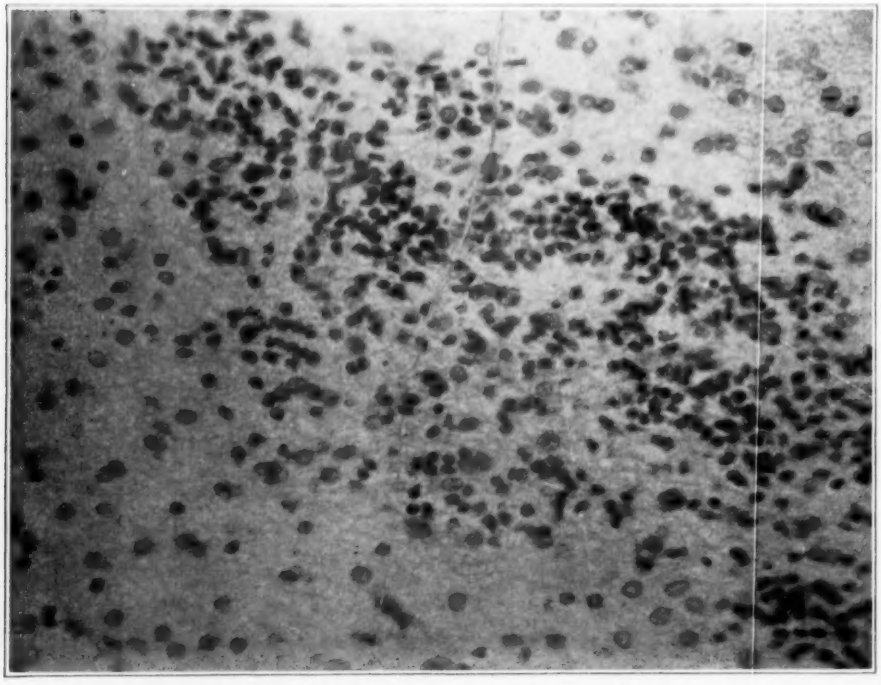

Fig. 2.—Mononuclear and polymorphonuclear leukocytes in the subependymal tissue of the left ventricle. Hematoxylin and eosin stain; × 300.

buccal mucous membranes were slightly more injected than usual. Neither the abdominal viscera nor the heart showed any abnormalities.

The left lung weighed 46 Gm. and was covered by a glistening pleura. Its anterior portion was pale pink and crepitated normally. A small portion of the lower part of the upper lobe and the whole of the lower lobe posteriorly was deep red, almost purple and firm. On section these consolidated masses extended, wedge-shaped, from the hilum of the lung toward the posterior surface, the base of the wedge being the posterior surface of the lung. These consolidated masses were engorged with blood and projected above the rest of the surface of the lung. The bronchi and bronchioles were free from mucous plugs and were lined by injected but intact mucosae.

The right lung weighed 43 Gm. It was a uniformly pale pink, crepitant organ, except for two small, dark red nodules of consolidation, one of which was at the very apex of the lung and measured 1.5 cm. in diameter. The rest of the lung showed no abnormality. The hilic lymph nodes were small and succulent.

Microscopic examination of the lungs showed the normal pulmonary markings in the areas of consolidation to be obliterated by a cellular exudate which filled the alveoli and bronchioles. This exudate was composed chiefly of polymorphonuclear leukocytes, but an occasional alveolus contained, in addition, a few mononuclear cells and homogeneously pink-staining material. Secondary pulmonary lobules composed of emphysematous alveoli lay adjacent to lobules which were completely filled with exudate as just described. The pleura was free from exudate. The epithelium lining the bronchioles was intact, but numerous polymorphonuclear leukocytes lay between the epithelial cells, as if arrested in their progress to the lumina. Large numbers of the cells forming the exudate had pyknotic nuclei, many of which were undergoing disintegration.

The cranial sutures were not separated, nor was there overriding of the cranial bones. The anterior fontanel was not bulging and measured 3 by 4 cm. The posterior fontanel was small. The calvarium was thin. Because the dura was firmly adherent to the cranial sutures, the brain was removed without the dura. There was no atrophy of the cerebral convolutions and no evidence of hemorrhage over the superior surfaces of the brain. There was, however, a subarachnoid hemorrhage at the base of the brain surrounding the left internal carotid artery and adjacent to the left optic nerve, to the left lateral side of the optic chiasm, and to the left oculomotor nerve. This hemorrhage was of small extent and was circumscribed. Its point of origin could not be determined with certainty; the left internal carotid artery and the larger meningeal vessels were intact. Further, because there were no petechial hemorrhages in the underlying cortical substance, the most likely seat of origin would appear to have been a torn pial vessel. There was no exudate in the meninges of either the brain or the spinal cord. Multiple sections of the brain and cord revealed no gross evidence of pathologic changes in either organ. Petechial hemorrhages were entirely absent.

The cranial sinuses and both middle ears were explored and found free from exudate.

Microscopic examination showed the meninges to be entirely free from any exudative reaction. Sections from both cerebral hemispheres showed diffusely scattered focal collections of small, deep staining mononuclear cells. Occasional mononuclear cells with large, pale, vesicular nuclei and abundant cytoplasm were also present in these cellular foci. Some cellular accumulations had sharp circular outlines which suggested that they lay within the blood vessels. No vessel walls, however, or limiting endothelial membranes could be discovered. The outlines of the individual cells on the periphery of these accumulations strongly suggested an infiltration of the brain substance. By far the largest collections lay at various distances from the ependyma lining the inferior horns of the lateral ventricles, although smaller collections were present in the corpus striatum of each hemisphere. Though these mononuclear cells not infrequently lay adjacent to cerebral vessels, nevertheless a true perivascular collection of cells as a "collar" was nowhere present. Interspersed among the mononuclear cells were occasional polymorphonuclear neutrophils. The ganglion cells of the entire cerebral cortex as well as of the hippocampi were well stained. Here and there a ganglion cell was surrounded by a clear space resembling edema. There were no hemorrhages present, and no abnormal glial cells were found. Microscopic examination of the pons, medulla and cord revealed no cellular reaction of any kind, and the nerve cells of these structures were well stained.

SUMMARY

The foregoing report is that of a white female infant, aged 4 months, who showed the clinical picture of whooping cough accompanied by neurologic signs suggestive of encephalitis. At autopsy, bilateral focal pneumonia, acute diffuse encephalitis and subarachnoid hemorrhage were found. The demonstration of acute encephalitis and a localized subarachnoid hemorrhage in a patient with whooping cough is of sufficient rarity to warrant this communication. No data are available in this case regarding the etiologic agent producing the inflammatory reaction in the brain; the pertussis infection may be directly or indirectly related to the lesions in the brain.

SICKLE CELL ANEMIA IN A GREEK FAMILY*

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AND
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DETROIT

On Dec. 7, 1928, Charles M., a Greek boy, aged 4 years, was brought to the outpatient department of the Children's Hospital because of anemia, enlarged spleen and jaundice.

The present illness, which had been noticed for more than a year, began with lassitude and anorexia. Slight jaundice was observed almost from the beginning, with no increase in intensity. The stools had been normal in color, and the urine possibly darker than before. There had been some loss in weight. A splenic tumor had been noticed for some months. There had been no vomiting and no hemorrhages from any part. The illness had not been severe enough to require putting the child to bed, or to keep him from play.

The history was essentially unimportant. The patient had been apparently normal in infancy, and had developed well, except for poor teeth. Measles had been the only acute illness. The tonsils had been removed. The parents came to America from Byregos, a small village in the Peloponnesus near Olympia, where their families had long been resident and where negroes are said to be unknown. Their four children were born in the United States. Both father and mother seemed well, the mother appearing especially robust. Of the four children, one died at the age of 9 months, of influenza; a girl, aged 13, was well, and Angelo, a boy, aged 14, had had an anemic condition for ten years, similar to that of Charles, for which he received treatment at Bellevue about eight years before the present examination. There was no suggestion of anything negroid in the coloring or features of any of the family.

The older boy, Angelo, who felt well and attended school regularly, accompanied his brother to the hospital. Their blood was examined at the same time. The first examinations were not complete, as it was expected that Charles would be admitted to the ward for further study.

The report of examinations of the blood made on December 7 was as follows:

Charles: Hemoglobin, 36 per cent; red blood cells, 3,170,000; white blood cells, 11,400; polymorphonuclears, 40; large mononuclears, 17; small mononuclears, 37; basophils, 1; eosinophils, 4; normalblasts, 1, and platelets, 132,000. Other observations were: marked anisocytosis and poikilocytosis; macrocytes and microcytes, and marked polychromatophilia.

Angelo: Hemoglobin, 46 per cent; red blood cells, 4,200,000; white blood cells, 14,200; polymorphonuclears, 46; large mononuclears, 21; small monoclears, 28; normoblasts, 2, and platelets, 220,000. Other observations were: marked anisocytosis and poikilocytosis; macrocytes and microcytes, and marked polychromatophilia.

In a study of stained smears of this boy's blood, elongated forms were seen (fig. 1) which, while not typical sickle cells, were so like some observed in sickle cell anemia as to arouse suspicion.

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* Submitted for publication, Feb. 4, 1929.

* From the Children's Hospital of Michigan.

Charles was admitted to the hospital on Dec. 12, 1928. Important points in the physical examination at that time were: pronounced pallor and slight jaundice; slight general enlargement of the superficial lymph nodes; poorly developed teeth; a short systolic murmur at the apex of the heart; a large, firm, smooth mass (spleen) in the left hypochondrium, extending three fingerbreaths below the margin of the rib, nearly to the midline anteriorly and well into the flank.

The blood at this time showed: hemoglobin, 30 per cent; red blood cells, 2,640,000; white blood cells, 11,200; polymorphonuclears, 38; large mononuclears, 18; small mononuclears, 35; eosinophils, 1, and normoblasts, 8. Other observations were: marked anisocytosis and poikilocytosis; moderate achromia; extreme poly-

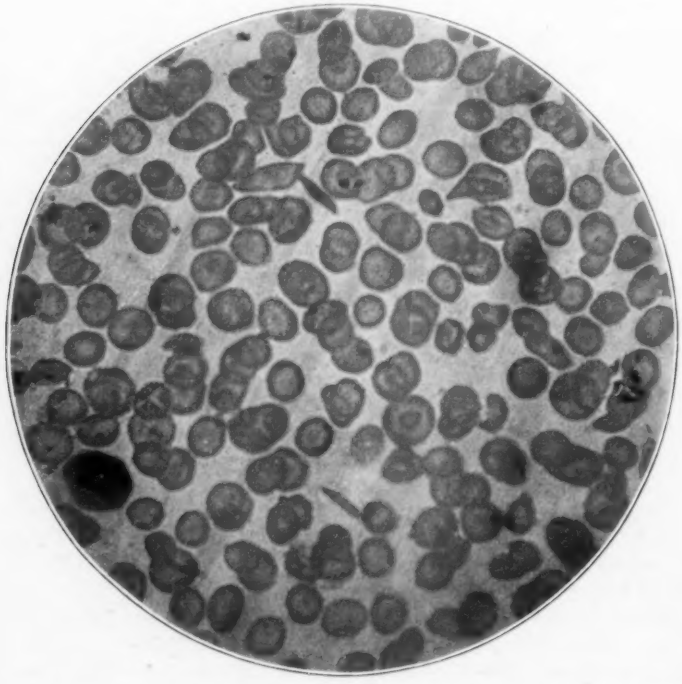

Fig. 1.—Stained smear of Angelo M.'s blood. Incomplete sickle cell formation.

chromatophilia, and reticulation, 30 per cent. In tests for fragility, hemolysis began at 0.3 per cent and was not complete at 0.2 per cent. The direct van den Bergh test gave a negative reaction, and that from the indirect tests was strongly positive. The icteric index was 24. The whole blood cholesterol was 152 mg., and lecithin, 78.7 mg.

Moist preparations of the blood showed a rapid and extreme development of sickle forms. Analysis of the gastric secretions showed achlorhydria. The urine contained small amounts of urobilinogen.

Roentgenograms of the skull and long bones showed nothing unusual.

As Angelo has never returned to the hospital we have not had an opportunity to study his case in detail.

The blood of the other members of the family was examined for sickle cells. That of the father and sister was negative, but the mother's blood showed a slow and incomplete development of sickle forms.

The father, who was quite intelligent, said that "trouble with the spleen" was a common complaint in the part of Greece where they had lived and that it was different from malaria, a disease with which he seemed to be well acquainted. The people apparently depend little on physicians, except in serious disease, but

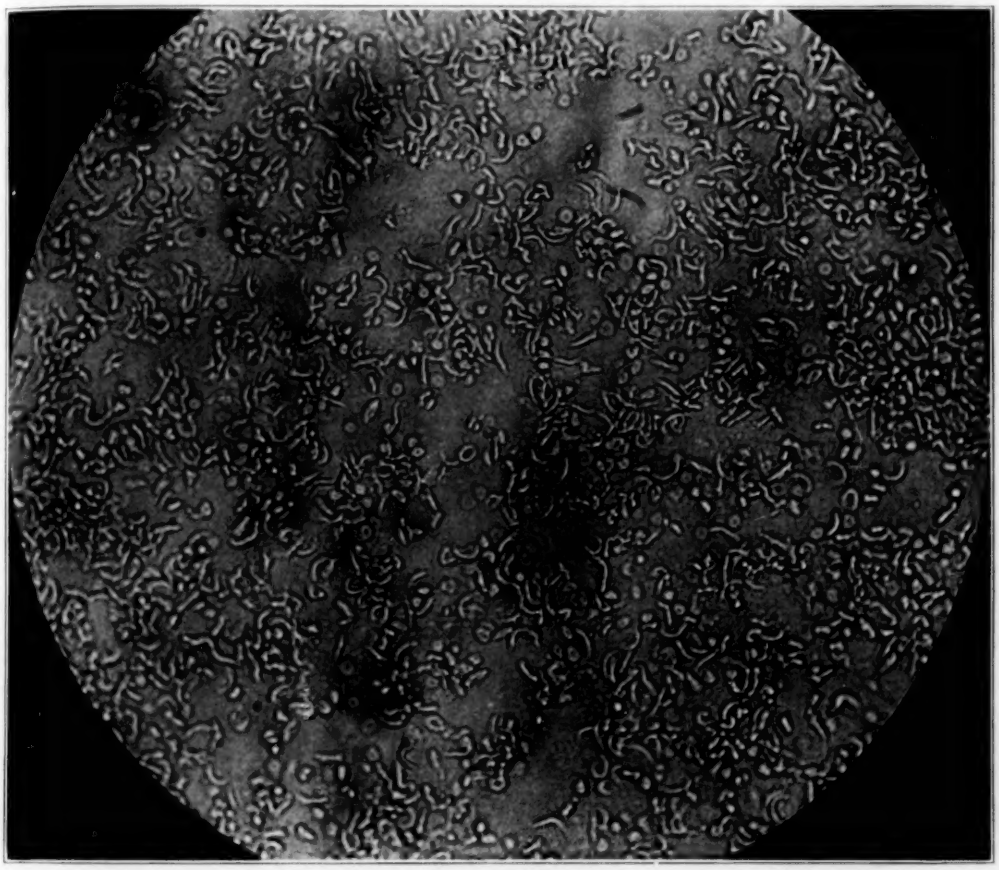

Fig. 2.—Moist preparation of Charles M.'s blood. Marked sickle cell formation.

treat themselves with their own concoctions of herbs. Neither husband nor wife could remember anything suggestive of splenic anemia in the wife's family.

COMMENT

So far as our knowledge goes, these are the first observations of definite sickle cell anemia in subjects regarding whom no reasonable suspicion can be raised of an admixture of negro blood. Unquestionably, the general acceptance of the dictum that sickle cell is peculiar to the

negro race has been too precipitate. This cell is not usually recognizable in ordinary stained smears, and requires for its detection a special technic not used in routine examinations of the blood. Until moist preparations of blood from persons of various races in all parts of the world have been studied, it will not be safe to say how common the characteristic is, nor what conditions govern its incidence and spread. Lawrence's [1] observation of unquestionable sickle cells in small numbers in the blood of various white people suggests that it must be quite a common condition; and that the characteristic anemia may prove to be more widely distributed than has been supposed. The demonstration that it is not peculiar to the negro race emphasizes further its resemblance to congenital hemolytic icterus, to which we have referred in previous articles; [2] while its occurrence in a Greek family might seem to cast doubt on some of the cases of a peculiar hemolytic disease which we have reported as practically limited to children of the Mediterranean races.[3] We examined the blood of only one of these patients [4] for sickle cells, which we did not find. It happens that none of the others is now within our reach. Rich,[5] in a recent article, referred to peculiarities in the histology of the spleen which he believed to be pathognomonic of the sickle cell subject. His paper was only a preliminary report without illustrations, and we are unable to conclude from our own observations whether the peculiarities he described would sufficiently distinguish the sickle cell condition from hemolytic icterus, which it closely resembles. Certainly, however, the sections of the spleen from our cases [6] of erythroblastic anemia are definitely different from what we have seen in sickle cell anemia. Hereafter, we shall feel obliged, however, to study the blood in all cases of hemolytic anemia for the formation of the sickle cells, as the clinical resemblances between these disorders are very close.

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1. Lawrence, J. S.: Elliptical and Sickle Shaped Erythrocytes in the Blood of White Persons, J. Clin. Investigation **5**:31 (Dec.) 1927.

2. Cooley, T. B.: Resemblances and Contrasts in the Hemolytic Anemias of Childhood, Am. J. Dis. Child. **36**:1257 (Dec.) 1928. Cooley, T. B.; Witwer, E. R., and Lee, P.: Anemia in Children with Splenomegaly and Peculiar Bone Changes, Am. J. Dis. Child. **34**:347 (Sep.) 1927.

3. Cooley, Witwer and Lee (footnote 2, second reference). Cooley, T. B.: Von Jaksh's Anemia, Am. J. Dis. Child. **33**:786 (May) 1927.

4. Cooley, Witwer and Lee (footnote 2, second reference, patient 4).

5. Rich: The Splenic Lesion in Sickle Cell Anemia, Bull. Johns Hopkins Hosp. **43**:398 (Dec.) 1928.

6. Cooley, Witwer and Lee (footnote 2, second reference, patients 2, 3 and 4).

CONGENITAL BACKWARD DISLOCATION OF THE KNEE*

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While the orthopedic textbooks occasionally mention the occurrence of a backward dislocation of the knee and state definitely that it is a more severe form of congenital genu recurvatum, the number of cases reported in the literature is small. It is only recently that these cases have received attention and that the details of the treatments have begun to appear in the literature. (A few cases were reported in the *Journal of Bone and Joint Surgery.*) This indicates that the deformity is not extremely rare, but merely is not reported.

In 1926 I reported one case,[1] and since then I have had another case. The same treatment was carried out in both instances, in the second case, however, with more speed. The recovery of both patients was complete and rapid. The principle of the treatment in these cases may prove of interest.

REPORT OF CASES

CASE 1.—M. S., a girl, the first child of healthy parents, born by a vertex presentation, without forceps, was seen by me on Sept. 16, 1925, when only 3 days of age. Examination showed a distinct recurved or hyperextended right knee. There was no marked contraction of the quadriceps tendon as the leg could be brought down to a straight angle but could not be flexed. There was a distinct groove above the patella. One could feel the patella.

The x-rays showed no abnormality, but, of course, a reliable interpretation of a radiogram could not be made for a patient of this age.

A small Thomas Jones splint was applied, with the knee in straight position and traction straps. In two weeks the splint was flexed slightly at the knee. The angle of flexion was gradually increased so that at the age of 6 weeks the leg was flexed at an acute angle. Massage was then instituted three times a week, the brace being removed at each treatment. When the child was 2 months of age, the brace was taken off for one hour twice a day. The time was gradually increased, so that at the age of 3 months (the time of the report) it was off for about four hours daily. At the age of 5 months the brace was dispensed with entirely. The infant was observed till about the age of 1 year when it commenced to walk.

When the child was seen in 1928, she was 3 years of age. She walked without a limp, and there was absolutely no difference in the contour or length of either limb.

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* Submitted for publication, March 25, 1929.

1. Boorstein, Samuel W.: Congenital Genu Recurvatum, M. J. & Rec. **124:** 541 (Nov. 3) 1926.

CASE 2.—J. F., a boy, was referred to me by Dr. A. Isaacson on Oct. 23, 1927, when 1 day old.

The family history was irrelevant. The patient was the second child of healthy parents. The delivery was normal, by a vertex presentation; no forceps were used. The deformity was noticed immediately after birth.

The physical examination showed a distinct dislocation of the left leg on the thigh, the leg being hyperextended to an angle of 120 degrees, that is 60 degrees beyond the normal fully extended knee. The condyles of the femur were felt in the popliteal space. A groove was present over the patella. It was found that the left knee could be flexed even with force only to an angle of 160 degrees.

J. F. (case 2), as observed in November, 1928, at the age of 1 year. A good position of the left knee is shown.

Complete flexion was prevented by contraction of the quadriceps muscle. As the patient was seen at home, a roentgenogram was not taken.

A small Thomas Jones leg splint with a half ring was applied. Traction was obtained by adhesive plaster and tape. By using a little force, the knee could be flexed to an angle of 150 degrees, 10 degrees more than before. A small felt pad was applied underneath the condyles of the femur to help push them anteriorly. The half ring permitted easy cleansing of the child.

On Oct. 28, 1927, that is, five days later, the splint was removed. The crease of the quadriceps muscle above the patella was markedly diminished, and the knee

could easily be flexed to a right angle. The splint was then bent to a right angle. A high foot post was put on at the end of the splint. The traction tapes were attached to this foot piece. Felt pads still were used under the condyles. The thickness of the pads was increased so that the condyles would be pushed forward.

On Nov. 2, 1927, when the brace was removed, the child could kick with the leg and the hyperextension did not return. Massage was ordered. The brace was discontinued and a flannel bandage was applied to keep the leg in acute flexion.

The patient was seen by me once or twice more. The deformity did not recur. The child commenced to walk at the age of 9 months.

The accompanying photograph, taken at the age of 1 year, shows the normal shape of the knee.

REVIEW OF LITERATURE

Whitman [2] advised: "Massage of the atrophied and contracted muscles, combined with more or less forcible manipulation in the direction of flexion." This is often combined with a simple posterior splint. "If there is more resistance, manual force may be applied under anesthesia, and the deformity may be overcome at one or several sittings, or the shortened tissues, particularly the tendon of the quadriceps or the ligamentum patellae may be lengthened at open operation. The limb is then fixed in a flexed position until the tendency to recurrence has been overcome. When the child begins to walk a light lateral brace may be necessary to ensure perfect functional use of the joint, as in many instances laxity of ligaments and muscular weakness may persist for a long time."

Albee [3] said: "In plain genu recurvatum, frequently repeated flexion of the leg may be practised, with retention of the flexed position in the interim of manipulations, using for this purpose a malleable iron splint with straps and buckles, and bending it from time to time to follow the increase of flexion. The manipulations should be supplemented by massage of the flexor muscles of the leg. Cases resisting this treatment demand section of the quadriceps tendon with shortening of the hamstring tendons. . . . If dislocation is present, an attempt should be made to reduce it, supplemented by tenotomy of the contracted quadriceps tendon if necessary, and by shortening of the hamstrings. If the dislocation persists after puberty, arthrodesis of the knee-joint may be indicated if the deformity offers an obstacle to walking."

Cochrane [4] advised: ". . . manipulation into the normal extended position and the application of a splint. This may be done under an anesthetic. The first maneuver is to draw the femur well forward on

2. Whitman, Royal: Orthopaedic Surgery, Philadelphia, Lea & Febiger, 1923.

3. Albee, Fred H.: Orthopaedic and Reconstruction Surgery, Philadelphia, W. B. Saunders Company, 1919.

4. Cochrane, W. A.: Orthopaedic Surgery, New York, William Wood & Company, 1926.

the tibia before flexing the joint. A series of manipulations may be necessary, gaining more and more flexion each time and fixing the limb upon a moulded posterior splint. When weight-bearing is begun, a knee cage should be worn to prevent hyperextension of the joint."

Lewin [5] used manipulation and application of a plaster of paris cast, or a splint made of plaster or other material, holding the knee in a flexed position.

Wentworth [6] reported a case of double congenital dislocation of the knees. "Recourse was made to slow flexible traction in the line of deformity, by means of an improvised double traction splint made with wire and padded. Traction was applied to the legs below the knees, and carried through rubber bands to the splints; countertraction, by means of padded wire peroneal pieces attached to splint. This permitted easy care of the child and gradual increase in the amount of flexion." Recovery was reported to be obtained in two months.

Griswold [7] reported a case in which reduction was performed. "Position was maintained by adhesive plaster, the adhesive being changed at frequent intervals, until the tenth day when all dressings were removed. No sign of recurrence was evident when patient was discharged two days later."

Baldwin [8] reported a case in which the treatment was delayed till the age of 10 days. The dislocation was reduced under anesthesia. "The knee was then flexed to nearly its normal limit. It was held in a position of about 90 degrees flexion on a plaster splint. There was a moderate reaction which lasted about one week. The splint was removed daily after the first few days for the purpose of cleanliness, but the knee was not allowed to extend. At the end of four weeks flexion was normal and extension was normal with no tendency toward recurrent dislocation. However, as a safeguard, a brace which permitted flexion but limited extension to within 45 degrees was used until the child was 6 months old. It could have been discarded safely at a much earlier period."

He emphasized the point that although the patella is not palpable on the dislocated knee, it develops later if the patient is treated early.

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5. Lewin, Philip: Orthopaedic Surgery for Nurses, Philadelphia, W. B. Saunders Company, 1928.

6. Wentworth, Edward T.: Gradual Reduction of Congenital Anteriorly Dislocated Knees, J. Bone & Joint Surg. **10**:585 (July) 1928.

7. Griswold, Arthur S.: Congenital Dislocation of the Knee Joint, J. Bone & Joint Surg. **9**:628, (Oct.) 1927.

8. Baldwin, C. H.: Congenital Dislocation of the Knee Joint, J. Bone & Joint Surg. **8**:822 (Oct.) 1926.

CONCLUSIONS

1. Patients with congenital dislocation of the knee and genu recurvatum should be treated as early as possible; the first day is not too soon.

2. The prognosis is good, and recovery can be obtained in from two to three weeks.

3. The treatment consists of gradual flexion of the knee, followed by massage.

4. A small Thomas Jones splint allows this method of treatment to be carried out with simplicity and ease.

Progress in Pediatrics

CONGENITAL HEART-BLOCK

REVIEW OF THE LITERATURE; REPORT OF A CASE WITH INCOMPLETE HETEROTAXY; THE ELECTROCARDIOGRAM IN DEXTROCARDIA *

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True congenital heart-block is rare. In 1920, Carter and Howland [1] reviewed the seven reasonably established cases previously reported and added one of their own. In 1921, White, Eustis and Kerr [2] added two more from the literature reported since the publication of Carter and Howland's review, and gave detailed accounts of two cases of theirs, one of which was undoubtedly congenital. In recording another case, Romberg and White [3] (1924) mentioned the cases of Bravo y Frias [4] (1922) and of Barbier, Lebée and Mouquin [5] (1922). Fourteen other cases have been recorded in the literature, one each by Meyer [6] (1923), Nobécourt [7] (1924), Wilson and Grant [8] (1925), McIntosh [9] (1927), Lukin and Frey [10] (1927), Davis [11] (1927), Gibson [12] (1927), Aldrich [13] (1927), Shapiro [14] (1927), Haverschmidt [15] (1928), Nissé [16] (1928), and Perotti [17] (1928), and two by Fleming and Stevenson [18] (1928). These twenty-nine cases, with the one in this report, include only those cases in which the diagnosis of congenital heart-block was sufficiently proved by the history and graphic methods.[19] These cases are shown in the accompanying table. The well studied case of de Massary and Lian [20] of incomplete heart-block first diagnosed when the patient was 34 might be added to the list, though it was not certain whether or not the condition had been present from birth. Many other cases are excluded either because of insufficient proof of their congenital origin or because of the existence of heart-block. These were reported by the following: Schuster,[21] von Starck,[22] Dunn,[23] Magnus-Alsleben,[24] Fleming and Kennedy,[25] Price and Mackenzie,[26] Heilhecker,[27] Armstrong and Mönckeberg,[28] Gill,[29] Zahorsky,[30] Frank and Polak,[31] Josué,[32] Eyster and Middleton,[33] Willius,[34] Leconte,[35] Calandre,[36] Lampard [37] (one case each); Morquio,[38] Volhard,[39] Hecht,[40] Aylward [41] (two cases each); and Clerc and Lévy [42] (four cases). Schlesinger [43] (1927) reported a case of congenital heart disease with right bundle-branch block which he thought was due to rheumatic myocarditis.

* Submitted for publication, Dec. 12, 1928.

* Work done in the Division of Medicine and the Section on Pathologic Anatomy, as a fellow in The Mayo Foundation, Rochester, Minn.

After the presence of heart-block has been established in a young patient by graphic methods, certain criteria are necessary to make the diagnosis of congenital, as opposed to acquired auriculoventricular dissociation. There must be some evidence of the existence of the slow pulse at a fairly early age and the absence of a history of any infection which might cause the condition after birth: notably, diphtheria, rheumatic fever, chorea and congenital syphilis. The occurrence of syncopal attacks at an early age is fairly good evidence of the existence of the heart-block prior to the attacks. Such evidence was present in five of the thirty accepted cases. The presence of signs of congenital heart disease, although not essential, adds weight to the congenital origin of the condition; but one must remember that congenital heart lesions, such as a patent interventricular septum, may be the seat of acquired endomyocarditis. In a review of twenty-one cases from the literature and one of their own, of auriculoventricular heart-block in children, Eyster and Middleton [33] (1920) considered the etiology of the condition to be distributed as follows: congenital in seven, questionably congenital in two, due to diphtheria in six, to rheumatism in one, to cardiac tumor in one, to bronchitis in one, pyogenic in one, questionably pyogenic in their case, and unknown in another. They considered as congenital several of the cases which have been excluded from the present review. In eleven of their twenty-one cases, Stokes-Adams' seizures unquestionably had occurred, and in two their occurrence was doubtful. Seham,[44] in a later review in Abt's "Pediatrics," stated:

> The first authentic heart-block reported was that of von Starck in 1903, but he did not take any records. Thirty-one cases of heart-block in children are reported in the literature. In seventeen, the heart block was complete; in five, partial, and in the remainder unspecified. The ages of these children range from fifteen months to fifteen years. In fourteen of the children there was a continuous, and in six a recurrent heart-block. The dissociation lasted from three days to eleven years in the majority of cases; however, the duration of the heart-block in the majority of cases was less than one year. Nine of the cases were associated with congenital lesions of the heart; nine, with diphtheria; two with rheumatism; one, with a cardiac tumor; one, with influenza; one, with congenital lues; one, with measles; and one was due to some pyogenic organism. Ten of the patients died, three were reported to have recovered, and the others were unaccounted for. The electrocardiograph or the polygraph were used in sixteen cases.

The occurrence of familial heart-block has never been proved. Fulton, Judson and Norris [45] (1910) reported "congenital heart-block occurring in a father and two children, one an infant." Without doubt the infant had congenital heart-block; but the father and the older child did not have heart-block, as a study of their polygraphic tracings shows. Aylward [41] (1928) reported two children of the same mother

who had pulse rates of from 40 to 60, but graphic records to prove the existence of heart-block were not made.

In regard to the time of discovery of the slow pulse in the thirty accepted cases of congenital heart-block, bradycardia was noted during the first year of life in eight instances; during the second year, in three; between the second and tenth years, in twelve; and between the tenth and twentieth years, in seven. In the first case of White, Eustis and Kerr,[2] the fetal heart beat was noted to be irregular eight hours before birth. In the case reported in this paper, the fetal heart beat was recognized to be slower than the mother's for two weeks before birth.

In these thirty-cases, the degree of auriculoventricular dissociation was complete in twenty-two; partial, in six; alternating between complete and incomplete, in one, and it was not determined in one. The last case was that of Perotti,[17] in which graphic records were not made but which is considered to be a case of heart-block because of the bradycardia noted since birth and because of the data obtained at necropsy.

The infrequency of cyanosis in this group of cases is noteworthy. It was entirely absent in fifteen, slight in nine, and marked in only six. The degree of cardiac hypertrophy was designated as none in two, questionable in three, slight in ten, moderate in seven and marked in eight.

Theoretically, two possibilities exist to explain the auriculoventricular dissociation in congenital heart-block; namely, prenatal endomyocarditis or syphilis involving the bundle of His, and developmental defects affecting the bundle of His. In only three of the thirty cases accepted in this review were studies made at postmortem. Of the others, patency in the interventricular septum was diagnosed clinically in sixteen instances and communication between the aorta and pulmonary artery just above the aortic valve, in one.

In two of the cases of patency of the interventricular septum, pulmonary stenosis was also thought to exist, and in a third the presence of this lesion was questionable. In one instance, pulmonary stenosis alone was diagnosed. In two cases cardiac murmurs were present which could not be interpreted. In four of the cases, clinical evidence of congenital heart disease other than the heart-block was not found, and in two cases mention of the cardiac examination was not made.

Two cases besides the one in this report came to necropsy. In that of Wilson and Grant,[8] in which incomplete heart-block was present, examination disclosed complete atresia of the root of the pulmonary artery, with a large, patent ductus arteriosus, and a common ventricle with only the rudiment of an interventricular septum in the form of a rounded, muscular prominence in the posterior wall. There was a nor-

Salient Data of the Thirty Cases of Congenital Heart-Block Resembling a Table of White, Eustis and Kerr

Case	Author	Sex	Age When Proved	Age When Slow Pulse Was First Noticed	Malformation	Cardiac Enlargement	Grade of Auriculo-ventricular Block	Slowest Ventricular Rate	Cyanosis	Other Observations
1	Van den Heuvel[19] (1908)	F	23 yrs.	15 yrs.	Patent interventricular septum	Marked	Complete	34	Slight	Attacks of syncope since the age of 2 years
2	Fulton, Judson and Norris[19] (1910)	M	22 mos.	7 days	Patent interventricular septum	Slight	Complete	42	Absent	Father and older child had normal rhythm and not heart block as reported
3	D'Espine and Cottin[19] (1915)	M	8 yrs.	8 yrs.	?	Slight	Complete	20	Absent	One attack of syncope
4	Whipham[19] (1915)	F	18 mos.	18 mos.	Patent interventricular septum	Slight	Partial 2:1	56	Absent	
5	Whipham[19] (1915)	F	12 yrs.	6 yrs.	Patent interventricular septum	Marked	Complete	40	Absent	
6	Bass[19] (1918)	M	13 yrs.	12 yrs.	?	Slight	2:1 and complete	37	Absent	
7	Gorter[19] (1919)	M	6 mos.	6 hrs.	?	?	Complete	60	Slight	
8	Rosenson[19] (1920)	F	10 yrs.	8 yrs.	Aortopulmonary patency	Marked	Complete	44	Absent	
9	Carter and Howland[1] (1920)	F	3 yrs.	3 yrs.	Patent interventricular septum	Slight	Complete	37	Absent	One attack of syncope at the age of 4 years
10*	Smith[19] (1921)	M	20 yrs.	20 yrs.	?	Slight	Complete	43	Absent	Attacks of syncope between the ages of 3 and 9 years
11	White, Eustis and Kerr[2] (1921)	F	4 days	8 hrs. prenatal	Patent interventricular septum	Marked	Partial 2:1 and less	70	Slight	Mongolian idiocy; marked right ventricular preponderance in electrocardiogram
12	White, Eustis and Kerr (1921)	M	6 yrs.	5.5 yrs.	?	Moderate	Complete	46	Slight on exercise	
13	Bravo y Frias[4] (1922)	F	5 yrs.	4 yrs.	?	Slight	Complete	43	Absent	Fever at 4 months with cerebral irritation
14	Barbier, Lebée and Mouquin[5] (1922)	M	15 yrs.	15 yrs.	Patent interventricular septum	Moderate	Complete	41	Absent	Infantile development; bony anomalies
15	Meyer[6] (1923)	F	18 yrs.	18 yrs.	Patent interventricular septum; pulmonary stenosis	Moderate	Complete	63	Marked	
16	Romberg and White[3] (1924)	F	9 mos.	9 mos.	Patent interventricular septum	None	Complete	50	Slight on crying	
17	Nobécourt[7] (1924)	M	10 mos.	10 mos.	Stenosis of pulmonary artery; patent interventricular septum	Marked	Complete	60	Slight on crying	
18	Wilson and Grant[8] (1925)	F	14 mos.	14 mos.	Absence of interventricular septum	Marked	Incomplete 2:1	66	Marked	Clubbed nose, fingers, toes; necropsy; histologic study
19	McIntosh[9] (1927)	F	7 mos.	7 mos.	Patent interventricular septum	Marked	Complete	57	Absent	
20	Lukin and Frey[10] (1927)	F	8 yrs.	7.5 yrs.	?	Slight	Complete	43	Absent	Influenza at 3 years; "weak heart" diagnosed
21	Davis[11] (1927)	?	13 mos.	13 mos.	?	?	Complete	45	Absent	
22	Gibson[12] (1927)	F	13 yrs.	9 yrs.	Patent interventricular septum	Slight	Complete	59	Slight	
23	Aldrich[13] (1927)	F	12 yrs.	4 yrs.	?	?	Partial, 3:1	45	Absent	Sudden death at 13 years
24	Shapiro[14] (1927)	F	9 yrs.	8 yrs.	Pulmonary stenosis	Moderate	Partial, 2:1	44	Marked	Sudden death
25	Haverschmidt[15] (1928)	..	2.5 yrs.	2.5 yrs.	Patent interventricular septum	Marked	Complete	55	Present on crying	
26	Nissé[16] (1928)	F	7 yrs.	23 mos.	Patent interventricular septum	Moderate	Complete	48	Absent	
27	Perotti[17] (1928)	F	.....	1 to 3 days	Patent interventricular septum	Slight	No graphic records	60	Slight	Necropsy; no histologic study
28	Fleming and Stevenson[18] (1928)	M	3.5 yrs.	21 mos.	Patent interventricular septum	Moderate	Complete	30	Absent	One attack of unconsciousness at 3¼ years
29	Fleming and Stevenson (1928)	F	8 yrs.	8 yrs.	Patent interventricular septum; pulmonary stenosis (?)	Moderate	Partial, 2:1	45	Marked	Frequent attacks of fainting since patient began to walk
30	Yater (1928)	M	2 days	2 wks. prenatal	Unusual congenital anomalies	None	Complete	47	Marked	Multiple congenital anomalies; necropsy; histologic study

* The absence of infections of any importance and the occurrence of syncopal attacks between the ages of 3 and 9 years are etiologic evidence in this case.

mal mitral valve, but the valve of the right ostium venosum had only a medial and a lateral cusp. Besides the anomalies of the heart, there was complete absence of the left kidney and a fused right kidney with two elements. Serial sections were made of the posterior part of the heart; they revealed a well developed auriculoventricular node in the interauricular septum between the coronary sinus and the central fibrous body. From the front of the node, two main strands of nodal tissue entered the dense fibrous tissue of the lower part of the central fibrous body, one from the right side of the node and one from the left side. The course of these two strands was difficult to trace through the fibrous tissue, since they repeatedly branched and became greatly reduced in size; some of these branches reunited, whereas others appeared to end blindly. The general trend, however, was forward and slightly downward through the fibrous body toward the upper end of the muscular prominence in the posterior wall of the common ventricle. Here the strands appeared to issue as a single narrow band under the thickened endocardium, gradually spreading out to form definite Purkinje fibers and a large right branch. The explanation of this condition will be discussed later.

In the case of Perotti, who was unable to obtain graphic records of the infant who died three days after birth, there was complete absence of the membranous portion of the interventricular septum; the ventricles communicated with each other, and the right auricle communicated with the left ventricle. Histologic examination was not made, but from the anomaly found it may be assumed that there was a developmental break in the course of the bundle of His. However, it must be noted that many instances of patency in the interventricular septum occur without apparent disturbance of auriculoventricular conduction.

REPORT OF CASE

History.—On Aug. 9, 1928, a boy was born with the aid of low forceps, at full term. The parents were normal. The mother had had one previous confinement three years before, and had given birth to a normal infant. The only significant fact noted during the second pregnancy was discovered by the attending physician; namely, that the fetal pulse, for two weeks before labor, was slower than the mother's pulse. Just after birth, the infant was cyanotic for a few hours and had slight twitchings of the hands, arms and muscles of the face. Fifteen cubic centimeters of whole blood was given intramuscularly. The weight at birth was 3,260 Gm. (7 pounds and 3 ounces). Examination at that time revealed the absence of the left external auditory canal with a rudimentary external ear. A short distance behind this nubbin was a small, shallow sinus discharging a small amount of thin, yellowish secretion. The left side of the face was underdeveloped and pulled toward the right. A dermoid was located at the temporal limbus of the left eye. The neck was poorly developed, especially on the left side. The lungs were apparently expanded. The heart sounds were difficult to hear but were most audible in the median line, and the rate was slow, about 60 each

minute, with occasional irregularity. There seemed to be a systolic murmur over the base of the heart. Subsequent examinations revealed enlargement in the left side of the abdomen which it was thought might be the left lobe of a transposed liver. Consequently, a roentgenogram of the stomach was made after the administration of barium sulphate. The stomach was found reversed. The heart was carefully studied again, but the decision was that it was in its normal position. Enlargement of the heart could not be made out by either general or roentgenographic examination. The systolic basal murmur became more pronounced, and on one examination a diastolic murmur of different quality also seemed to be present. Electrocardiograms were taken on the second and sixth days. The first revealed heart block but was not satisfactory. The second showed complete auriculoventricular dissociation with an auricular rate of 116 and a ventricular rate of 47; the P wave was inverted in lead I, exaggerated in lead III and notched in all leads; the QRS complex was notched in lead III, and the T wave was diphasic in lead III (fig. 1).

The diagnosis in this case was as follows: (1) rudimentary left ear, (2) branchial cleft sinus, (3) imperfect development of the face and neck; (4) dermoid of the left eye, (5) congenital cardiac lesion with heart-block and (6) transposition of the abdominal viscera.

The infant was placed on a feeding formula of equal parts of milk and water with 10 per cent Karo syrup. It took its bottle quite well for a time. During the first days it lost weight, but by the end of the eleventh day it had regained its birth weight; after this, however, it gradually lost again. Following a feeding, slight cyanosis would appear for a short time; this became more pronounced at successive feedings. The pulse rate remained persistently low, usually between 60 and 70. The temperature was always normal.

On the eighteenth day, the infant died; the cyanosis had become quite marked by this time.

Necropsy.—The entire body was markedly cyanotic when examined five hours after death. The congenital anomalies of the head, face and neck were noted. When the peritoneal cavity was opened, complete situs inversus of the abdominal viscera was found (fig. 2). The liver was large and almost filled both upper quadrants, but the lobe on the left side was larger and the gallbladder lay to the left of the median line. When the pleural cavity was opened, the left lung was found to have three well-defined lobes, and the right, two lobes. The heart occupied the middle of the thorax (fig. 3). Its general outline was square, but the apex undoubtedly lay at the left lower angle. The transverse width was 5 cm., and from the inferior edge to the upper border of the auricles the distance was about 5 cm. also. A coronary artery was seen running vertically down the middle of the ventricular portion of the heart. The aorta lay on the right side; the pulmonary artery was to the left and on about the same plane. The aorta curved first somewhat to the right, then slightly to the left at the upper portion of its arch, and finally backward and downward to the right along the right side of the vertebral column. The pulmonary artery gave rise to two branches, the right of which passed under the arch of the aorta. An auricular appendage lay above each ventricle on each side of the great vessels.

The heart was removed and opened along the usual lines, except that the opening was made in the reverse order. The reason for this was that as the back of the heart was inspected, the great veins were seen to empty into the auricle, which was joined to the left ventricle. The organ with the great vessels attached weighed 47 Gm. The auricle on the left side had one appendage which

passed forward and medially as usual, and another smaller appendage or recess, posterior and medial, passing to the right a little beyond the median line and overlapping slightly the auricle which lay to its right and received the pulmonary veins. The latter recess did not contain pectinate muscles. The superior vena cava emptied into the auricle on the left in the usual manner; shortly above its mouth it became two veins, but the course of these had not been determined before removal of the viscera. The usual crista terminalis was found in this auricle, and the architecture was similar in most respects to that of a normal right auricle. The inferior vena cava opened into it in the usual way, except that it was transposed; a eustachian valve could not be demonstrated for this vein. Instead of a common coronary sinus there were two venous openings below the

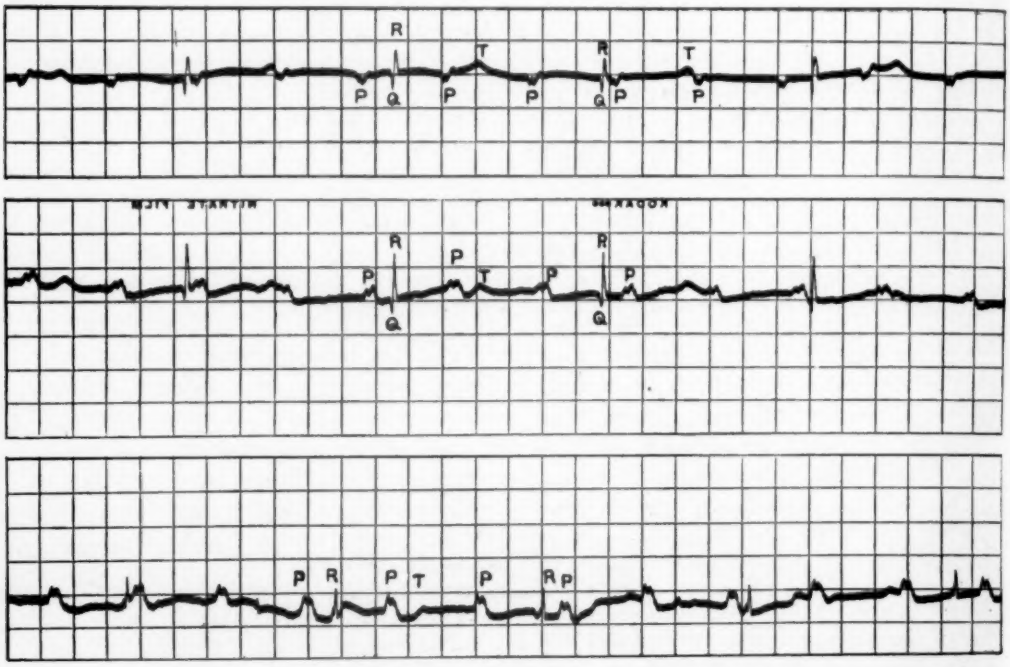

Fig. 1.—Electrocardiogram taken on the sixth day of life in the case reported in this paper.

orifice of the inferior vena cava, one lying above the other. The upper one was the opening of the vein coming from the left along the auriculoventricular sulcus; the other, of the vein coming from the right. The limbus fossae ovalis was well marked on this side of the auricular septum and was roughly triangular. A fenestrated membrane lay on the under side of the septum across the anterior half of the foramen ovale. The little recess previously mentioned, which overlapped the medial side of the auricle on the right posteriorly, lay to the right of the orifice of the inferior vena cava and at its upper angle received a vein that lay just to the right of the two right pulmonary veins, the three lying close together. The left auriculoventricular orifice was apparently of normal size, 2.7 cm. in circumference; it was well formed and had a normal mitral valve with an anterior and a posterior papillary muscle.

Fig. 2.—The viscera removed in toto in the case reported in this paper.

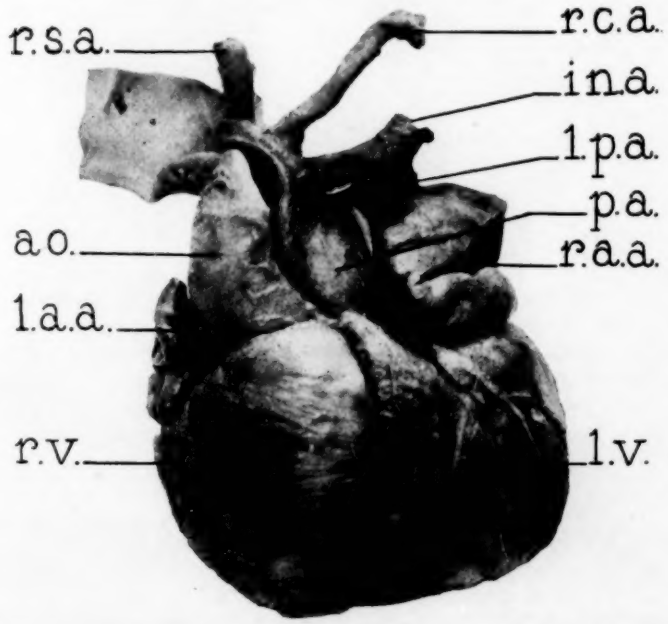

Fig. 3.—Anterior aspect of the removed heart. *l.v.* indicates the left ventricle; *r.v.*, right ventricle; *l.a.a.*, left auricular appendage; *r.a.a.*, right auricular appendage; *ao.*, aorta; *in.a.*, innominate artery; *r.c.a.*, right carotid artery; *r.s.a.*, right subclavian artery; *p.a.*, pulmonary artery; *l.p.a.*, left pulmonary artery.

The ventricle was the typical adult left ventricle, and at the base of the pulmonary artery, which arose from it, was a normal membranous septum to which the "aortic" cusp of the mitral valve was attached (fig. 4). The wall of the ventricle was thick (4.5 mm.) but of only normal thickness for an infant of this age, and the cavity appeared to be of the proper size, 3 cm. deep. The ventricular septum was normal except for a small communication through its muscular portion, near its anterior edge, a short distance below the membranous septum. A probe, about 1.5 mm. in diameter, could be passed through this canal and entered the right ventricle in the infundibulum. The pulmonary artery arose where the aorta should have arisen; it had only two semilunar cusps, a right and a left, with small corpora arantii. The right cusp was 1 cm. long transversely; the left, 1.3 cm. Just above the right cusp was a saclike pocket about 1.5 mm.

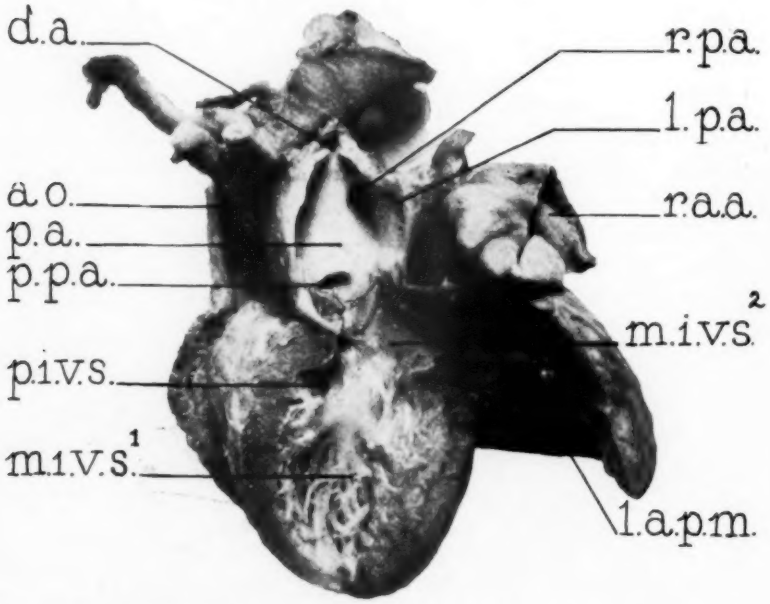

Fig. 4.—The left ventricle opened to expose the origin of the pulmonary artery. *r.a.a.* indicates the right auricular appendage; *m.i.v.s.*[1], muscular portion of interventricular septum, left side; *p.i.v.s.*, patency in interventricular septum; *m.iv.s.*[2], membranous portion of interventricular septum; *l.a.p.m.*, left anterior papillary muscle; *p.a.*, pulmonary artery; *p.p.a.*, pocket in pulmonary artery; *l.p.a.*, left pulmonary artery; *r.p.a.*, right pulmonary artery; *d.a.*, patent ductus arteriosus; *ao.*, aorta.

deep. The pulmonary artery passed slightly backward, but soon divided into large right and left branches, the right of which passed under the arch of the aorta. A patent ductus arteriosus passed upward, above and to the right of the orifice of the right branch to its usual site in the aorta. The diameter of the probe which could be inserted through the ductus was about 2 mm.

The auricle which lay on the right side had an auricular appendage with a long, teatlike process anteriorly. Posteriorly, the cavity of the auricle extended con-

siderably to the left and was anterior to and overlapped somewhat by the transposed right auricle. At the extreme left angle in the roof of the cavity, two pulmonary veins emptied in close proximity. Two more veins emptied about the middle of the auricle and just to the left of a similar vein which emptied into the right auricle, as previously described. About two thirds of the foramen ovale was covered by a large, fenestrated semilunar membrane attached anteriorly, superiorly and inferiorly on the right side of the foramen ovale. The "left" auricle led into a normal right ventricle through a normal right auriculoventricular orifice, 3 cm. in circumference. The orifice had a normal tricuspid valve with three leaflets (fig. 5). The largest papillary muscle was on the anterior surface of the ventricle, between the anterior and posterior cusps, and there were several small papillary bundles on the septal and posterior walls. The anterior end of the medial or septal cusp and the left end of the anterior cusps were bound directly

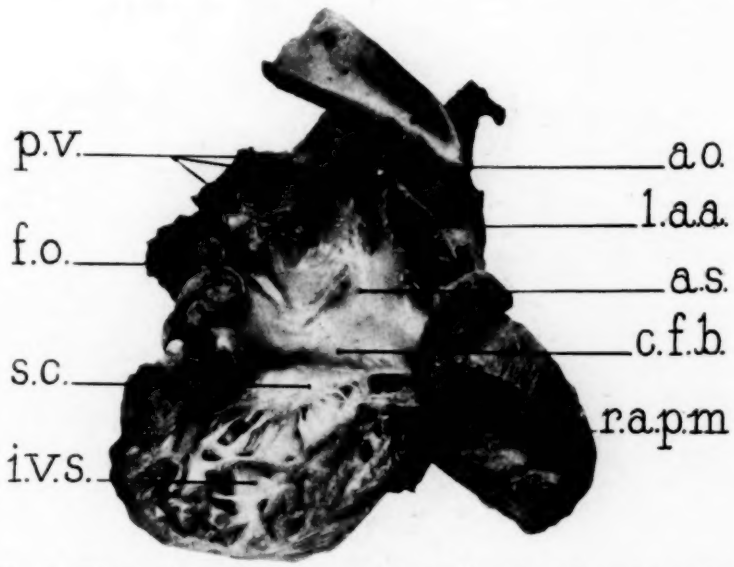

Fig. 5.—Right side of the heart opened, showing the left auricle and right ventricle. *a.s.* indicates the interauricular septum; *p.v.*, pulmonary veins; *l.a.a.*, body; *s.c.*, septal cusp of the tricuspid valve; *r.a.p.m.*, right anterior papillary left auricular appendage; *f.o.*, patent foramen ovale; *c.f.b.*, site of central fibrous muscle; *i.v.s.*, interventricular septum, right side; *ao.*, aorta.

to the wall of the ventricle, below the crista supraventricularis, by chordae tendineae. By transmitted light, the central fibrous body was seen to be in the normal position in relation to the tricuspid orifice, that is, above the medial (septal) cusp and part of the anterior cusp of the valve. The walls of the right ventricle were of about the same thickness (5 mm.) as those of the left. This cavity, which was 3 cm. deep, contained the usual infundibulum, from which, however, the aorta branched off directly (fig. 6). The aortic orifice was 1.9 cm. in diameter and was guarded by one posterior and two anterior semilunar cusps possessing large corpora arantii. The left coronary artery branched off from the left anterior sinus of Valsalva and apparently had the usual course. The orifice

of the right coronary artery was behind the posterior cusp, and this artery likewise apparently had a normal course. The noncoronary cusp was slightly smaller than the other two. Just above the point where the right pulmonary artery passed under the arch of the aorta, the innominate artery arose from the aorta on its left side. It gave rise to a left subclavian and a common carotid artery. A little farther along the arch, the right common carotid and subclavian arteries were given off separately.

Dissection of the walls of the ventricles under the dissecting microscope showed the muscular layers to be arranged in a manner similar to those of the normal heart.

The anatomic diagnosis was: developmental anomalies of the head and neck; transposition of all of the viscera and great vessels except the ventricles of the

Fig. 6.—Heart opened to show the infundibulum and origin of the aorta. *ao.* indicates the aorta; *p.a.*, pulmonary artery; *c.a.*, anterior descending branch of the left coronary artery; *r.a.a.*, right auricular appendage; *r.v.*, anterior wall of right ventricle; *l.v.*, left ventricle.

heart; patent ductus arteriosus; patent foramen ovale; small patency in the interventricular septum; two semilunar cusps in the pulmonary artery.

Histologic Examination.—From the standpoint of embryology, the most logical assumption regarding the situation of the sino-auricular node was that it lay in the wall of the auricle of the left side, which structurally corresponded to the right auricle. On the other hand, it was thought that the auriculoventricular node, most likely would be located in the right side of the interauricular septum and therefore in the auricle receiving the pulmonary veins, maintaining its relation to the central fibrous body. Acting on these assumptions, the examiners cut a long, narrow block of tissue from the groove in the auricle of the left side below the mouth of the superior vena cava, the groove apparently representing the sulcus

terminalis; and another larger block of tissue was removed from the septum of the heart, including the lower part of the interauricular septum and the upper part of the interventricular septum, both the membranous and muscular portions. Serial sections, 8 microns thick, were made through these two blocks of tissue; the first section began at the mouth of the superior vena cava, the sections being cut at a right angle to the sulcus terminalis; starting from the left of the other block as viewed from the right side of the septum, the sections were cut at a right angle to the annulus fibrosis. The blocks were embedded in paraffin. Every fifteenth section was mounted and was stained by van Gieson's method; the intervening sections were mounted and stained as desired.

The two nodes were found in the regions which it was expected would contain them. The sino-auricular node was therefore in the left side of the heart; the auriculoventricular, in the right. The sino-auricular node, cut transversely, was easily recognized by its fusiform shape, the connective tissue framework, the delicacy and interlacing of the fibers, and the central artery (fig. 7). It differed from the adult node only in being closely surrounded by the auricular muscle fibers. It lay just beneath the epicardium, in the sulcus terminalis, with many subepicardial nerves and ganglions in the vicinity.

The auriculoventricular node lay close against the right side of the central fibrous body in the auricle of the right side. The fibers were more slender and more loosely bound together than the auricular muscle fibers. They were also interlaced more. Here, again, the muscle fibers of the auricle were closely applied to the periphery of the node. The artery normally seen in the node was not present in this instance. As this node was followed along in the sections, a point was reached where a small part of the node apparently was separated off by the central fibrous body, this part lying below the central fibrous body (fig. 8). In order to make certain of this cleavage, all of the sections in this portion were mounted and stained. The observation was verified—the node was actually separated at its anterior end into a larger portion above and on the right side of the central fibrous body and a smaller portion below. The upper portion quickly faded out in this position; the smaller, lower portion soon became larger, assumed an oval outline on cross-section and undoubtedly was the auriculoventricular bundle (fig. 9). This at first lay in the upper edge of the muscular portion of the interventricular septum, nearer the right side. It gradually became round (figs. 10 and 11) on cross-section and passed slowly over toward the left side of the septum, where it became oval again and ended as the left bundle-branch (fig. 12). A right bundle-branch could not be found.

Blocks of tissue also were removed from both sides of the interventricular septum and sectioned transversely. In the block removed from the left side of the septum, Purkinje fibers were easily recognized beneath the endocardium, but in the block from the right side, fibers suggestive of the right bundle-branch could not be found.

COMMENT

The structure of this heart was so unusual that one may well ask whether it is not possible that the ventricles as well as the auricles were transposed, and whether they were not merely the seat of various anomalies which caused each to resemble the opposite chamber. There are several reasons why this is not so: (1) The apex pointed to the left and was formed by the ventricle on the left; (2) the auriculoventricular

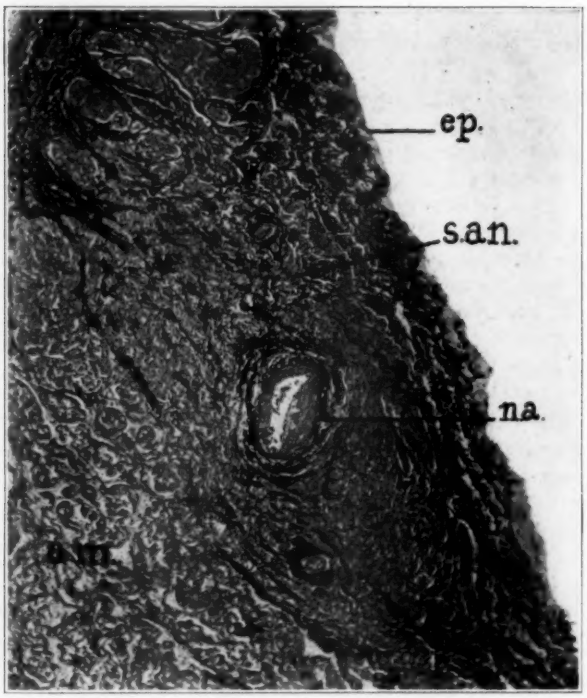

Fig. 7.—Microscopic section of the sino-auricular node cut transversely (× 40). *e.p.* indicates the epicardium; *s.a.n.*, sino-auricular node; *n.a.*, nodal artery; *a.m.*, auricular muscle.

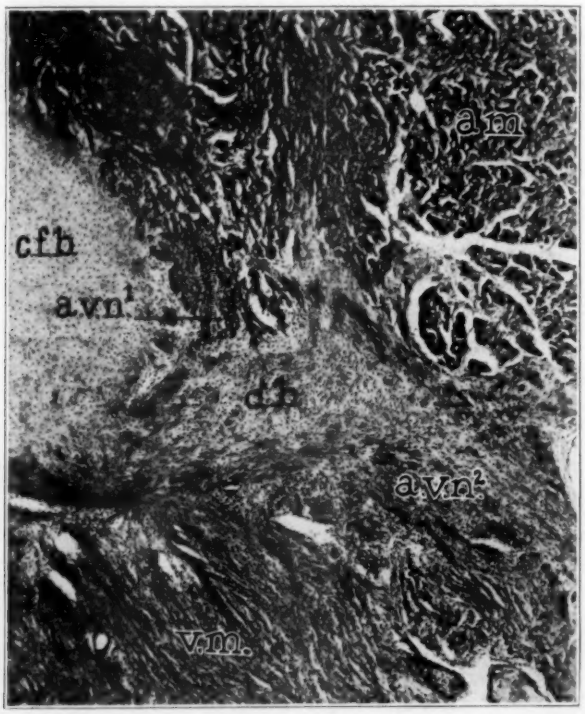

Fig. 8.—Microscopic section through central fibrous body, showing the auriculoventricular node divided by fibrous tissue. *c.f.b.* indicates the central fibrous body; *a.v.n.*[1], main part of auriculoventricular node separated by bridge of fibrous tissue, *d.b.*, from the smaller portion of the node, *a.v.n.*[2]; *a.m.*, auricular muscles; *v.m.*, ventricular muscle.

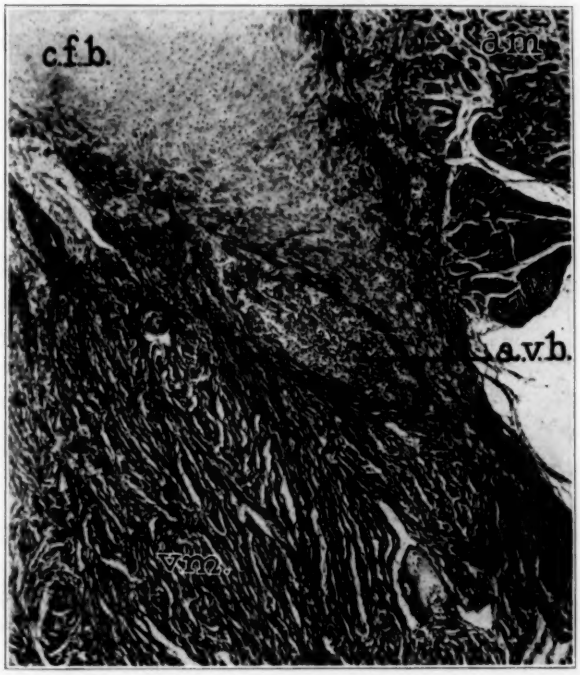

Fig. 9.—Microscopic section showing the first portion of the bundle of His (× 40). *c.f.b.* indicates the central fibrous body; *a.v.b.*, auriculoventricular bundle in cross-section; *a.m.*, auricular muscle; *v.m.*, ventricular muscle.

Fig. 10.—Microscopic section showing the bundle of His at about its middle (× 40). *c.f.d.* indicates the central fibrous body; *a.v.b.*, auriculoventricular bundle in cross-section.

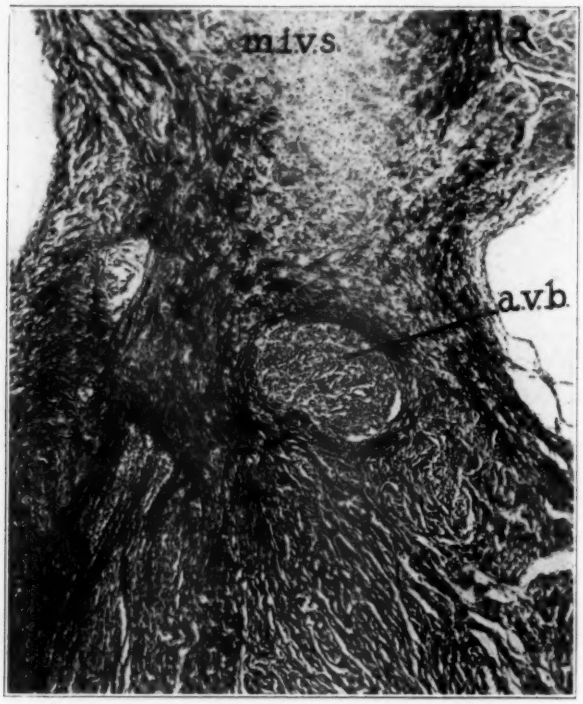

Fig. 11.—Microscopic section through the upper portion of the interventricular septum showing the bundle of His just before it gives off the left bundle-branch (× 40). *m.i.v.s.*, indicates the membranous portion of the interventricular septum; *a.v.b.*, auriculoventricular bundle in cross-section.

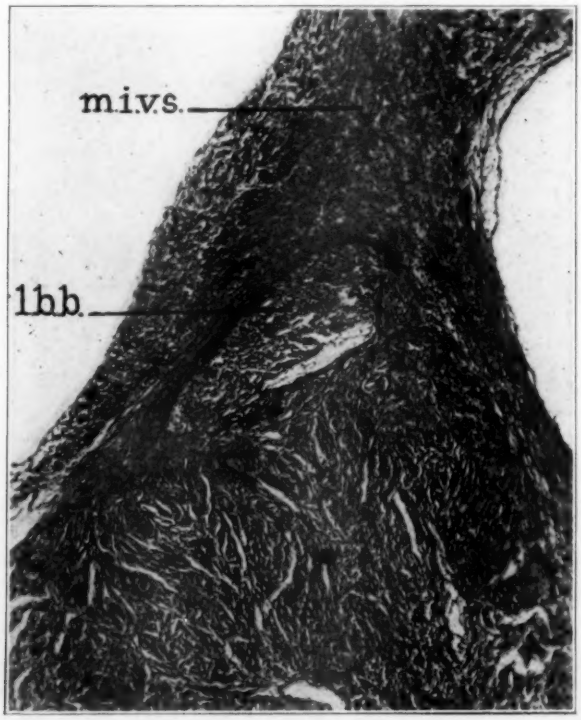

Fig. 12.—Microscopic section through the upper portion of the interventricular septum, showing the origin of the left bundle-branch (× 40). *m.i.v.s.*, indicates the membranous portion of the interventricular septum; *l.b.b.*, left bundle-branch origin.

valve of the ventricle on the left was the typical adult type of mitral valve with its two papillary muscles, and (3) the auriculoventricular valve of the ventricle on the right was the typical adult type of tricuspid valve with the usual papillary muscles of this valve; (4) the membranous portion of the interventricular septum lay in the ventricle on the left, and the conus arteriosus was in the ventricle on the right; (5) the arrangement of the musculature of the ventricles was similar to that in normally placed ventricles; (6) the auriculoventricular node was located in the right side of the heart, and (7) a case of complete transposition of the viscera has not been recorded in which there has been any doubt regarding the inversion of the ventricles because of anomalies in the structure of these chambers. The nomenclature suggested by Nagel [46] in cases of dextrocardia cannot be applied in such a case as this, nor indeed in any of the cases reviewed later in the paper. Nagel suggested that, in describing cases of dextrocardia, for purposes of orientation the ventricles should be called the caval ventricle and the pulmonary vein ventricle, according to the veins which emptied into the auricle that was attached to each ventricle, and not according to the character of the auriculoventricular valves, the arterial trunk arising from the ventricle or the position of the ventricles with reference to each other.

A similar case of transposition of the viscera has never been recorded. This one was unique in that there was complete situs inversus except for the cardiac ventricles. The heart was essentially completely developed except for the presence of certain minor anomalies. The only case reports of incomplete heterotaxy bearing any similarity to this one which could be found were those of Hickman [47] (1869), T. W. Griffith [48] (1892), J. P. C. Griffith [49] (1899), Fingerhuth [50] (quoted by Geipel in 1903), McCrae [51] (1905), Royer and Wilson [52] (1908) and Keith and MacDonnell [53] (1921).

In Hickman's case all the abdominal viscera except the cecum were transposed, and the course of the colon was irregular. The ventricles of the heart lay in their normal position, but the right auricle emptied into the left ventricle and the left auricle into the right ventricle. The aorta arose from the infundibulum of the right ventricle and arched to the left, passing down the left side of the spinal column along with the inferior vena cava. The ductus arteriosus gave rise to the right and left pulmonary arteries; the main pulmonary artery was represented by a fibrous cord which passed downward toward the heart from the ductus arteriosus on the inner side of the origin of the aorta. There was a defect in the interventricular septum. The case reported by J. P. C. Griffith was not far different from the one reported here. The only real points of difference were stenosis of the trunk and orifice of the pulmonary artery and a large defect in the upper portion of the

interventricular septum. The ductus arteriosus was not patulous throughout. The infant lived eight months and died of pneumonia. In Fingerhuth's case there was complete transposition of the viscera except for the aorta and pulmonary artery, which arose from a common cavity. McCrae reviewed briefly the subject of transposition with cardiac malformations and described an infant that lived forty-nine days. All of the viscera were transposed except the gallbladder. Although the apex of the heart pointed to the left, there was transposition of all of its parts. The normal right auricle and ventricle which lay behind and to the left were small, however, and a fibrous cord represented the pulmonary artery; the lungs were supplied by the right and left pulmonary arteries from the aorta through the ductus arteriosus. The interauricular septum was poorly developed. T. W. Griffith had previously described a similar case, in which, however, the interventricular septum was defective. In the case reported by Royer and Wilson there was transposition of all of the abdominal and thoracic viscera, but the heart was malformed. The greater part of the heart lay on the left side and the anterior portion was the right ventricle, from which both the aorta and the pulmonary artery arose. The aorta came from the uppermost part of the cavity, in front of and to the right of the pulmonary artery; and its descending portion passed downward along the right side of the vertebral column. Both carotids arose from separate trunks. The pulmonary artery did not have valves. The left ventricle was rudimentary and lay on the posterior aspect of the left border of the heart. The left auricle was large, receiving the venae cavae and the coronary sinus, and the left auriculoventricular orifice possessed only a single valve leaflet. The foramen ovale was wide open, leading into a smaller right auricle which received five pulmonary veins. The right auriculoventricular orifice contained a tricuspid valve. The fibrous portion of the interventricular septum was not present, and there was a large opening in the muscular portion. The ductus arteriosus could not be found. Keith and MacDonnell described a case of complete situs inversus of the viscera associated with dextrocardia, the heart lying on the right with its apex pointing to the right. The auricles were transposed, but the ventricles, auriculoventricular valves and stems of the great trunks were not transposed; at their origins, however, the aorta and pulmonary arteries had themselves undergone transposition or reversed torsion, so that the aorta arose from the right or tricuspid ventricle and the pulmonary artery from the left or mitral ventricle. Veins did not enter the auricle on the right side, but the venae cavae and pulmonary veins emptied into a common sinus venosus on the left, which led into the left auricle. Both the systemic and the pulmonary blood returned, therefore, through the left auricle, and the mixed blood was pumped from the heart by the left ventricle through

the much dilated pulmonary artery, which supplied the systemic circulation through a small ductus arteriosus.

I shall not attempt to explain the mechanism of development of such bizarre products of nature. As a rule, when both the abdominal and the thoracic viscera are transposed the transposition is complete, and complete situs inversus is much more common than either transposition of the abdominal viscera alone or dextrocardia alone (Arneill,[54] LeWald[55]). In situs partialis, the transposition of the abdominal organs may be irregular. Dextrocardia is the rarest of all forms of transposition (Nagel).

The cause of the heart-block in this case is obvious. The fact that the sino-auricular node was located in the opposite side of the heart from the auriculoventricular node did not have a bearing on the cause of the dissociation of auricular and ventricular rhythm, since the musculature of the auricles is, in the main, a common one; and whatever may be the point of origin of an impulse in the auricles, it will reach the auriculoventricular node quickly. In this case, however, the impulse from the sino-auricular node having been received by the auriculoventricular node, its passage along the auriculoventricular bundle was impossible because of the complete anatomic separation of the node from the bundle. The QRST, or ventricular, complex of the electrocardiogram was of the supraventricular form, indicating that the independently originated ventricular impulse arose high in the bundle of His. The inversion of the P wave in lead I was evidence of the abnormal site of origin of the auricular impulse, in this case the misplaced sino-auricular node. My inability to demonstrate a right bundle-branch in the histologic study was unfortunate. One feels that there must have been a right bundle-branch, since the ventricular complex was not of the form suggesting a right bundle-branch block, and since embryologically it is difficult to believe that there should not have been a right bundle-branch when both the main bundle and the left bundle-branch were present.

The case of Wilson and Grant was the only other case of congenital heart-block which has been studied histologically. These authors attempted to explain their data in the light of embryologic observations. In their case the interventricular septum was almost entirely absent, and the bundle of His was broken up into many strands which passed through a mass of fibrous tissue. It had been shown that the position of the auriculoventricular bundle on the upper border of the interventricular septum or on the posterior wall of the heart, respectively, is the usual one in hearts in which the septum is partially or wholly deficient (Keith,[56] Mönckeberg[57]). Subdivision of the bundle in its passage through the central fibrous body also had been noted in a case of subaortic septal defect (Mönckeberg). "Both embryologically

(Mall [58]) and comparatively (Keith and Flack [59]), the auriculoventricular bundle apparently represents the remnant of the ring of the atrial canal joining the auricles and ventricles. In the human embryo this ring is broken anteriorly and laterally in the formation of the mitral and tricuspid valves. According to Mall, the remnant holds a constant position just behind the posterior endocardial cushion, immediately over the septum of the ventricle, a position which is marked first by the interventricular foramen and later by the membranous septum. Mall further states that in the destruction of the lateral and anterior walls of the atrial canal not only does the endocardial thickening (of the cushions) play a rôle but also the connective tissue of the epicardium. This last forms a collar encircling the auriculoventricular groove, and as the mitral and tricuspid valves develop, the epicardial connective tissue is drawn into them, thus completing the separation of the atrial and ventricular musculature. Posteriorly it encircles the auriculoventricular bundle so that this becomes lodged between the posterior endocardial cushion and the outer connective tissue."

Wilson and Grant concluded from these observations that in their case there had been greater destruction of the tissue of the atrial canal than normally occurs, and that conduction through the bundle of His had been interfered with not only because of its separation into fine strands but because these strands were encased in fibrous tissue which compressed them.

The case reported here is, of course, quite different from theirs; but the embryologic observations which they used in their explanation are not inappropriate. Whatever may have been the cause of the failure of the ventricles to become transposed along with the remainder of the circulatory system, it acted early in embryonic life and probably during the period when the auricles were being separated from the ventricles. The bundle had developed in its normal position, but with the change in relationship which later occurred the auricles and ventricles became completely separated posteriorly as well as anteriorly. In this way, the bundle was completely severed in its upper portion.

The form of the electrocardiogram in this case suggested to Willius the question as to the cause of the inversion of the QRST complex in cases of situs inversus. In all cases of situs inversus in which the heart has been transposed, this complex, as well as the P wave, has been inverted in lead I. This electrocardiographic picture has been noted in cases of situs inversus by Waller,[60] Nicolai,[61] Hoke,[62] Owen,[63] Samojloff,[64] Neuhof,[65] De Castro,[66] Willius,[67] Funk and Singer,[68] LeWald,[55] Potts and Ashman,[69] and others. In all but a few of these cases there was little question that the situs inversus was complete and that the heart was transposed so as to represent the mirror image of the normally placed heart. Hirschfelder,[70] in his book,

"Diseases of the Heart and Aorta," showed the photograph of an electrocardiogram with upright complexes in lead I, which is claimed to be from a case of dextrocardia; but the author did not specifically mention this case, and similar cases have not been recorded in the literature. It may be assumed, therefore, that in cases in which the heart represents the mirror image of the normal heart the complexes in lead I are always inverted. In these cases the direction of the impulse along the bundle of His is to the right instead of to the left.

Furthermore, in cases of so-called dextrocardia due to displacement of the heart by intrathoracic extracardial conditions, this electrocardiographic picture is not seen. In such cases the heart is merely pushed or pulled to the right en masse, so that there is only a slight change in the direction of the true cardiac axis, that change often being a greater obliquity of the axis toward the right (Stone [71]). The direction of the impulse along the bundle of His is still to the left. In only one proved case has there been an actual dextroversion due to acquired disease, a case recorded by Lafforgue [72] (1902), in which as the result of a stab wound in the chest there was an accumulation of 5 liters of blood in the left side of the thoracic cavity. This fluid had pushed the heart to the right, and the apex was actually pointing to the right; but the torsion of the heart had so twisted the vessels that the lumen of the aorta was reduced to one-third the normal diameter. This patient lived only two months after the infliction of the stab wound, and an electrocardiogram was not obtained.

Nagel has shown that in the only proved cases of pure congenital dextrocardia, which are very few, the heart does not represent the mirror image of the normal beat; the apex is formed by the right or pulmonary vein ventricle, which lies posterior to the left or caval ventricle. In such cases the condition is apparently due to an arrest in that stage of development of the heart (six weeks) when this organ lies perpendicularly in the chest with preponderance of the right half of the common ventricle and with the apex formed by the future right ventricle. In such cases, the direction of the impulse along the bundle of His is to the right; unfortunately, electrocardiographic records have not been obtained. It may be said, nevertheless, that in all cases in which the axis of the heart actually has been directed to the right and the impulse along the auriculoventricular bundle was in that direction, when electrocardiograms were obtainable, the complex was found to be inverted. In the case of incomplete transposition which I have reported, this complex was upright and the direction of the impulse anatomically was toward the left. This fact constitutes proof, therefore, but of a negative character, that it is the reverse direction of the impulse along the conduction pathway that causes the inversion of the QRST complex.

Waller [60] conceived the idea that the direction of the complex was determined by the direction of the long axis of the heart, whereas Clerc and Bobrie,[73] and Vaquez and Donzelot [74] maintained that it was determined by the inversion of the ventricles. The long axis of the heart usually does correspond to the direction of the impulse along the bundle of His, but this relationship might not always be true. Vaquez and Donzelot were opposed to this theory on the basis of two cases which they studied clinically, in which, roentgenographically, the long axis was to the right and the complexes in lead I were upright. It is conceivable, however, that the true axis of the ventricles in these cases was to the left, and this point could be determined only by necropsy. Inversion of the ventricles produces a change in the direction of both the long axis and the path of conduction, but in the case of pure congenital dextrocardia the ventricles are not inverted, whereas both the long axis of the heart and the conduction bundle are inverted. The crucial point in the settlement of the cause of the inversion of the complexes of the electrocardiogram rests, therefore, on the form of the electrocardiogram in pure congenital dextrocardia, but this is unknown. It seems most probable, in view of all of the facts at hand, that it is the direction of the path of conduction along the bundle of His which produces the inversion of the QRST complex in lead I in cases of transposition.

SUMMARY AND CONCLUSIONS

Congenital heart-block is rare; only thirty cases, including the present one, have been reported. It is possible that some of the other cases considered as congenital heart-block by their reporters were actual cases of the condition, but the criteria in these instances are not sufficiently fulfilled. The occurrence of familial heart-block has never been proved.

Of the thirty cases of heart-block accepted as congenital, only three have come to necropsy, and in only two have histologic studies been made.

Either prenatal endomyocarditis or a developmental defect in the auriculoventricular bundle theoretically may cause the condition, but in the cases studied postmortem only the latter has been found.

The case reported in this paper is even more unique as an example of incomplete heterotaxy than as one of congenital heart-block.

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Pediatric Biographies

RICHARD WISEMAN
1622-1676

JOHN RUHRÄH, M.D.
BALTIMORE

This rather picturesque contemporary of Sydenham, Seargent-Surgeon Wiseman, is included among pediatricians, not because of his work among children in general, but for his account of the "King's Evil."

He was doubtless a Londoner, born about 1622. Just where he was educated is uncertain, but there is a record of his apprenticeship in the records of the Barber-Surgeon's Company, about 1637:

"Of Richard Smith, Surgeon, for Richard Wiseman, ij.s. vj d."

He began his career as a naval surgeon in the Dutch navy, and later he was an army surgeon, serving under Charles I at the siege of Weymouth. When the Prince of Wales was made King, he went with him to Scotland. He was close to him on various occasions. He had an exciting career, leaving the army when the King's forces were defeated at Worcester, after which he went to London, obtained his freedom from the Company of Barber-Surgeons, started as an assistant to "a most excellent chirurgeon" by the name of Molins, and later established himself in the Old Bayley at the Sign of the King's-head.

He was arrested on a false charge of trying to aid in the escape of a Royalist prisoner in the Tower, but after some months of incarceration he was released. After serving again as a naval surgeon for Spain, he returned to London, where he was practicing when Charles II returned. Ten days later, he was made "Surgeon in ordinary for the Person"; the next year he was King's Surgeon, and in 1672, "Our principall Chirurgion and our Sergeant-Chirurgion."

He died of some pulmonary disorder, and was buried in St. Paul's in Covent Garden. The record reads "29th Aug. 1676, Richard Wiseman, in the upper end of the Church." His life by Sir Thomas Longmore is well worth reading.

He wrote chiefly on surgical subjects, and his works went through seven editions. His essay on the "King's Evil" was published after his first venture had proved a success. It was difficult in those days to publish a book, as it needed "approvals." This one passed the licensing bishop (think of having to ask permission of a bishop to publish a medical book!), the Barber-Surgeon's, and what was more important, it received the approval of the Royal College of Physicians.

His account of tuberculosis is extremely good. To obtain a cure he advised first regulation of the diet, fresh air and hygienic measures, then certain drugs of no value and surgical measures when indicated. He was a good observer. "Before you open them you must endeavor at a perfect concoction; for if you open them while any part of the

Richard Wiseman, A. D. 1600. From a miniature in the possession of His Grace the Duke of Rutland.

Gland is hard, it will increase and put you upon a necessity of eradicating it." He would have had a hard time under our present regimen (referring to adults):

"An their Drink medicated Ale or Beer; Wine is also allowed, but Water utterly forbidden."

Wiseman was an educated man, and wrote much better English than the average medical man of his time. The following on the distribution of the lesions is illustrative:

The Parts usually affected in this Disease are either the Glands, Muscles, Viscera, Membranes, Tendons, or Bones. I don't remember ever to have seen the Nerves or Brain immediately affected with it; or if they are, it does not appear in the Shape of a Tumour, but rather dissolves and corrodes them, as it does the Marrow and Bones; in which Case the Disease gets another Name, and being mortal needs to be insisted on here.

The Veins and Arteries are no otherwise affected here, then they are in other Cases of Tumours.

The Glands are the principal Seat of this Distemper, insomuch that most Authors have confined it to them intirely. They indeed are most commonly affected in strumous Patients; and if the external and more visible ones remains whole, yet generally speaking the internal Glands, especially those of the Mesentery, are swelled and obstructed. Of these I have seen many different Examples, especially in Children, and have passed my Judgment, that they have been strumous when the external Signs were not quite so evident as to make others believe it; yet it hath appeared upon Dissection, that I was in the right. Nay, whenever the external Glands appear swelled, we may safely conclude those of the Mesentery to be so too, that being usually the first Part that is attacked in this Disease. Nor is this peculiar to the Mesentery alone, but likewise all the conglobate Glands suffer along with it, as is evident in those of the Groin, Axillae, &c. but no where more frequently than in the Neck. Nor are the conglomerate Glands exempted from the same Malady, such as the Glandulae Salivales, Tonsillae, Lachrymales, the Thymus, the Pancreas, the Mammae, the Testicles, Prostatae, &c.

These are sometimes affected together with the conglobate Glands, sometimes separately. In some we have found all the Conglobate Glands of the Neck swelled, and many of them pressing hard upon, and between the Salivals; yet they remained sound.

So likewise the Pancreas and Thymus have been surrounded with Strumae, while they themselves have remained unaffected. But very often the Conglomerate Glands suffer by themselves, as in the Ranula, which is a Tumour of the Glandula Salivalis inferior. The Parotis also, or the external Salical Gland, is very often preter-naturally affected: And in the Pancreas, the learned Dr. Needham says, he had seen a strumous Tumour suppurated, which held a Pint of Matter, while the Glands of the Mesentery remained quite sound.

That the Breasts are evidently subject to the Scrophula, sufficiently appears from Common Experience.

I can give no Instance of this Disease in the Testicles or Prostatae; but perhaps this may be owing to our generally suspecting another Distemper, when these Parts come to be affected with Tumours.

News and Comment

SOCIETY NEWS

World Conference for Crippled Children.—Edgar F. Allen, president of the International Society for Crippled Children, announces a world conference for crippled children at Geneva, Switzerland, from July 28 to August 2.

Cuban Pediatric Society.—The Proceedings of the Cuban Pediatric Society has been received. The volume is well gotten up and does credit to its editors, Dr. Aballi and Dr. Hurtado.

UNIVERSITY NEWS

Dr. Park Receives Honorary Degree.—Dr. William H. Park, well known expert on contagious diseases, has been granted this year the honorary degree of Doctor of Science by Yale University.

Appointments and Promotions.—The following appointments, effective July 1, 1929, have been made at the University of California Medical School: W. A. Reilly and Minola Stallings, instructors in pediatrics. The following members of the faculty were promoted: C. F. Gelston and E. B. Shaw from instructors in pediatrics to assistant clinical professors of pediatrics.

CARE OF CHILDREN BETWEEN THE AGES OF 1 AND 6 YEARS IN HOLLAND

Among large portions of the population of Holland there has been a long felt need for an organized supervision of the health of the child between the ages of 1 and 6 years. On May 24 and 25 of this year a special congress was held in Amsterdam to discuss the matter. A large number of social and medical associations and authorities sent their representatives, and the congress was opened by the state minister for public health. Several medical authorities and social workers threw light on the manifold sides of the problem of the care of the child between the ages of 1 and 6 years.

Among the several subjects which were treated at the congress may be mentioned the discussion as to how to make an exact survey of the morbidity of little children and in what way the numerous diseases of children of this age could be best combated (acute infectious diseases, especially measles and whooping cough, and tuberculosis, rickets, orthopedic deformities and diseases of the teeth). Then the conditions for a proper school for these children were discussed, what food should be given, what difficulties had to be overcome in sending the little children into the country, how the homes of these children should be arranged and, finally and most important, in what way a proper organization could be developed.

As a result of the congress, a committee will be formed out of the represented organizations which will be charged with the formation of propositions for the organization of preventive care of the child between the ages of 1 and 6 years, and which will take into account the important discussions of the congress.

PERSONAL

Dr. Edmond A. Lesné has been made an honorary member of the Academy of Medecine of Paris.

GENERAL

Mothers' Milk Registry.—A mothers' milk registry was opened at Pittsburgh in March in quarters provided by the Magee Hospital.

BENJAMIN KNOX RACHFORD, M.D.
1857-1929

Obituary

BENJAMIN KNOX RACHFORD, M.D.
1857-1929

Dr. Benjamin Knox Rachford died in Cincinnati on May 5, 1929. He was born in Alexandria, Ky., on Nov. 28, 1857. Both his grandfather and his father were physicians. Dr. Rachford was graduated from the Medical College of Ohio in 1882, receiving at that time the faculty prize, a gold medal and the Joseph Ransohoff gold medal for excellence in descriptive anatomy. His internship was served in the Cincinnati General Hospital. For a time he practiced in Alexandria, Ky., and in 1888 he moved to Newport, Ky. In 1894 he moved to Cincinnati where, three years later, he married Gretchen Louise Wherry, daughter of Gen. William M. Wherry, U.S.A.

Dr. Rachford held the following positions: In 1888 he was quiz master and assistant to Prof. J. C. Whittaker; in 1893 he was offered the position of associate professor of physiology at Harvard, which he declined; in 1894 he was made professor of bacteriology in the Ohio Medical College, and in 1895 professor of physiology, which chair he filled until 1898. In 1897 he was offered the chair of pediatrics in the College of Physicians and Surgeons in Chicago, which he declined after considerable deliberation. In 1897 he was elected director of pediatrics in the Cincinnati General Hospital, and was given control of the outpatient dispensary. In 1898 he was made professor of materia medica and therapeutics; he held this position until 1901 at which time he took over the chair of pediatrics; he continued in this latter position until 1920. In 1908, and for twelve years thereafter, he was president of the medical staff of the Cincinnati General Hospital.

Dr. Rachford's work falls more or less naturally into four groups. In 1890, while working in the laboratory of Professor Gad in Berlin, he discovered a method of creating a pancreatic fistula in rabbits and obtained pure pancreatic juice. This led to pioneer work on the pancreatic juice which has remained a classic in physiology. Next, Dr. Rachford became interested in the neuroses of childhood and made many contributions to this subject. Later, he made valuable studies in typhoid, diphtheria and other subjects related to public health. Finally, he was a real pioneer in preventive pediatrics—not only contributing freely to the literature on this most important phase of medicine, but organizing the pediatric department at the University of Cincinnati in a way which has served as a model for other institutions. The pediatric

department of the University of Cincinnati was endowed by Mrs. Mary M. Emery, and is known as the B. K. Rachford Department of Pediatrics. His greatest contribution to preventive pediatrics was his remarkable work in the organization and functioning of the Babies' Milk Fund Association in Cincinnati.

Dr. Rachford was the author of a textbook on the diseases of children, and of two other books, "The Neuroses of Childhood" and "Some Physiological Factors of the Neuroses of Childhood." In addition, he contributed more than sixty articles to the literature.

Dr. Rachford was a member, and at one time president, of the American Pediatric Society. He was a member of the Association of American Physicians. At one time he was a member of the committee of revision of the Pharmacopeia.

It can truthfully be said that Dr. Rachford was one of the great men of medicine. His influence for good was not confined to pediatrics, but he was one of the builders of the College of Medicine of the University of Cincinnati, interesting himself and others in this project. His work was always carried on with courage and with great self-sacrifice and devotion. As a practitioner he was kind, gentle and sympathetic, and he was loved both by his patients, and by all the numerous members of the medical profession who came in contact with him. His inspiration for what was good and right will be a stimulation to those who will try to carry on his great work.

A. G. M.

Abstracts from Current Literature

Anatomy and Physiology

FREQUENCY AND DISTRIBUTION OF FOSSA PHARYNGEA IN HUMAN CRANIA. HENRY B. COLLINS, JR., Am. J. Phys. Anthrop. **11**:101, 1927.

Human craniums to the number of 9,135 in the U. S. National Museum were examined, and the frequency of the fossa pharyngea noted. As to sex, the fossae were distributed as follows: females, 6.55 per cent; males, 4.98 per cent; children, both sexes, 5.35 per cent. The Melanesians show the highest frequency of the fossa; the white races, the lowest. Among American Indians the highest frequency is found among the Shoshonean-speaking tribes, followed closely by the Sioux, Apache, and other Plains tribes, and the Aleutians. The Eskimos show the lowest frequency of any American group.

[ARCH. PATH.]

THE SIGNIFICANCE OF THE CONCENTRIC CORPUSCLES OF HASSALL. HARVEY ERNEST JORDAN and GUY WINSTON HORSLEY, Anat. Rec. **35**:279 (June) 1927.

Histologic evidence is presented for an interpretation of the concentric corpuscles of the thymus in terms of foci of occlusion of capillaries and precapillary arterioles following endothelial-cell hypertrophy in involution. Structures closely resembling Hassall's corpuscles of the thymus, and clearly representing segments of precapillary arterioles in which the lumen has become obliterated through hypertrophy of the endothelium, are described in the case of certain involuting lymph nodes of the rabbit.

[ARCH. PATH.]

IS PITUITARY SECRETION CONCERNED IN THE INHERITANCE OF BODY-SIZE? R. CUMMING ROBB, Proc. Nat. Acad. Sc. **14**:394 (May) 1928.

A comparison was made of the weights of the pituitary bodies in giant (Flemish) and dwarf (Polish) male rabbits and in their F_1 hybrids. There is no characteristic difference in the weight of the pituitary body that may be correlated with the differences observed in growth rate. With increase in body weight, a progressive decrease in relative pituitary weight occurs. In the full-grown dwarf rabbit, accordingly, there is relatively twice the amount of pituitary substance observed in the adult Flemish giant rabbit.

COBB, Boston.

Pathology, Bacteriology and Biochemistry

THE PASSAGE OF LIVING BACTERIA THROUGH THE INTESTINAL WALL. LLOYD ARNOLD, Am. J. Hyg. **8**:604, 1928.

The bacterial flora of the small intestine can be altered by diet and also by climatic changes. Disturbances in the heat regulatory mechanism on the animal cause a qualitative and quantitative difference in the flora of the upper half of the small intestine. These changes are intimately associated with an inhibition of the normal bactericidal power of the small intestine. This allows the cecal flora to ascend into the upper part of the alimentary tract, and interferes with the destruction of ingested bacteria.

Sudden alkalinization of the upper part of the small intestine, in the presence of certain kinds of protein material or bile, allows viable bacteria to pass through the wall of the intestinal tract and appear for a short period of time in the thoracic duct. It is thought that these changes are brought about by alterations in the equilibrium of the autonomic nervous system.

[ARCH. PATH.]

PRECIPITIN REACTIONS WITH VARIOUS TISSUES OF ASCARIS LUMBRICOIDES AND RELATED HELMINTHS. GRAEME A. CANNING, Am. J. Hyg. **9**:207, 1929.

The data presented here indicate that certain isolated tissues, due to their composition and embryonic origin, are preeminently fitted to use in performing immunologic tests to trace biologic relationships of animals, whereas others not only are unsuitable but would tend to confuse the results. Thus, more delicate specific differences may be discovered between various ascarids by the use of a substance, like the egg, whereas more distant relations may be revealed by the use of sperm. From these things it follows that it is far better to find the most suitable tissue than to use the whole worm when conflicting elements would obscure the results.

[ARCH. PATH.]

COD LIVER OIL FOR REPRODUCTION. V. E. NELSON, E. OHRBECK, R. L. JONES and M. W. TAYLOR, Am. J. Physiol. **85**:476, 1928.

A commercial brand of cod liver oil was found to furnish an adequate supply, in rats, of the fat-soluble vitamin and of vitamin E, greatly surpassing butter fat in these respects. Seventh generation rats were successfully raised with 5 per cent of this cod liver oil furnishing the only source in the diet of vitamins A, D and E. One per cent was found to supply enough vitamin E to permit ready reproduction. On the synthetic diets many of the females died at time of parturition or shortly after delivery. The fetuses and young in these cases were normal. With diets associated with failure of reproduction there was no evidence that anemia was the cause of sterility.

THE EFFECTS OF CARBON ARC RADIATION ON THE BLOOD OF DOGS. H. S. MAYERSON and H. LAURENS, Am. J. Physiol. **86**:1, 1928.

Following a single exposure (abdominal) to carbon arc radiation, there was observed in dogs a temporary increase in plasma volume of from 6 to 37 per cent, with recovery to normal in five hours. Further exposures caused recurrence, but not augmentation, of this dilution; the duration, however, varied with the strength of exposure and the interval between successive exposures. After massive exposures, the initial dilution was followed by a slight concentration. Repeated exposures resulted in a stimulation of the hematopoietic system, indicated by an increase in the red cell count of from 10 to 19 per cent, lasting from three to six weeks. The red cells during the postradiation period were smaller and less saturated with hemoglobin. Blood platelets diminished in number and volume during irradiation, usually with recovery within five hours. Occasionally there was an increase during the postradiation period. A progressive leukopenia, with a marked lowering of the white cell count during the postradiation period, developed during irradiation.

THE EFFECT OF LIGATION OF THE COMMON BILE DUCT UPON THE APPEARANCE OF TETANY IN THYROPARATHYROIDECTOMIZED DOGS. J. C. BROUGHER, Am. J. Physiol. **86**:39, 1928.

In dogs, ligation of the common bile duct, with or without cholecystectomy, prevents the development of typical parathyroid tetany. This may occur in mild form, in which case its onset is delayed. This delay may be explained in several ways: a lessened excretion of calcium which would otherwise occur in the bile; increased absorption of calcium from the intestine because of the absence of the alkaline bile salts by which calcium is precipitated, and depression of the central nervous system by the absorbed bile.

THE PENETRATION OF ULTRAVIOLET RAYS INTO LIVE ANIMAL TISSUE. W. T. ANDERSON, JR., and D. I. MACHT, Am. J. Physiol. **86**:320, 1928.

The passage of ultraviolet light, of wavelengths of from 2,537 to 3,000 Angstrom units, was studied in the partially detached, but living, skin of the rabbit by means

of fluorescent photometry. It was found that there was a transmission of from 6 to 10 per cent through a skin 1.2 mm. thick. With the onset of death of the skin, there was definite reduction in transparency, and dead skin of the same thickness was found to be practically opaque to ultraviolet light shorter than 3,660 Angstrom units.

THE VALUE OF ACTEROL (IRRADIATED CHOLESTEROL) IN THE TREATMENT OF THYROPARATHYROIDECTOMIZED DOGS. J. C. BROUGHER, Am. J. Physiol. **86**:538, 1928.

The onset of a violent attack of tetany is prevented in parathyroidectomized dogs by the administration of 0.4 cc. of irradiated cholesterol in the presence of milk. Absence of the latter as a source of calcium renders the irradiated cholesterol without effect. Irradiated cholesterol induces more rapid recovery time than does cod liver oil, from fifteen to thirty days for the former, and from thirty to forty days for the latter. Apparently, a large supply of vitamin D is effective in many instances to enable the body to use calcium in the condition of parathyroid tetany.

RICKETS AND TETANY IN RATS. A. T. SHOHL and F. C. BING, Am. J. Physiol. **86**:633, 1928.

While correction of the defective mineral metabolism of rickets in rats could be accomplished by two essentially opposed methods — by the use of cod liver oil or irradiated food on the one hand, and by the addition of phosphates to the diet on the other — the animals to which the phosphates were administered showed a temporary hyperirritability of the neuromuscular system which was lacking in the others.

H. E. EGGERS.

ON THE TIME OF ABSORPTION AND EXCRETION OF BORIC ACID IN MAN. L. KAHLENBERG and N. BARWASSER, J. Biol. Chem. **79**:405, 1928.

Boric acid passes through living skin with remarkable ease and rapidity. The carefully cleaned feet of three adult men were immersed in a saturated, aqueous solution of boric acid, held at 45 C. Samples of the urine were drawn from each subject at intervals of five and fifteen seconds and examined for the presence of borates. Traces were found, invariably, within from fifty to fifty-five seconds of the moment of immersion.

ARTHUR LOCKE.

THE ARTERIAL SUPPLY OF THE CONGENITAL POLYCYSTIC KIDNEY. G. BAEHR and S. A. RITTER, J. Clin. Investigation **6**:19, 1928.

The clinical course of patients with bilateral cystic kidneys may be uneventful until late in adult life, but attacks of lumbar pain commonly occur, sometimes followed by persistent hematuria. By the method described, barium sulphate and gelatin are injected into the arterial supply of the kidneys; after the organs are cleared in methyl salicylate, they are studied by stereoroentgenograms. The arteries in the walls of the cysts are found to be stretched, and sometimes extend across the cavities, enveloped in a thin falciform fold of the cyst wall. Rupture of these arteries occurs from various causes resulting in a hemorrhagic cyst. If this cyst ruptures into a calyx, hematuria occurs; if it ruptures at the surface of the kidney, a perirenal hematuria is produced. Sclerosis of the arterioles or small arteries of the kidneys and other organs develops usually in the third decade, but occasionally as late as the sixth decade of life. This gives the same clinical picture in its evolution as primary arteriosclerosis, or the late stage of chronic glomerulonephritis following nephritic edema.

THE PROTEIN CONTENT OF THE CEREBROSPINAL FLUID IN MYXEDEMA. W. O. THOMPSON, P. K. THOMPSON, E. SILVEUS and M. E. DAILEY, J. Clin. Investigation **6**:251, 1928.

In seventeen cases of myxedema, the protein concentration of the spinal fluid was found to be high. It usually dropped to normal limits with the administra-

tion of thyroid extract. A differential point is thus given in the rare case in which myxedema may be confused with tumor of the brain or with chronic nephritis.

H. R. FISHBACK.

INFLUENCE OF LIGHT ENVIRONMENT ON THE GROWTH AND NUTRITION OF NORMAL RABBITS WITH ESPECIAL REFERENCE TO THE ACTION OF NEON LIGHT. WADE H. BROWN, J. Exper. Med. **48**:31 and 57, 1928.

The influence of light environment on the growth and nutrition of normal rabbits was studied by comparing the weight curves of animals living under different environmental conditions for periods of from four to eight months and the effects of change from one environment to another. Prolonged exposure to neon light was compared with confinement in the dark and exposure to diffuse, filtered sunlight of varying intensity. The results of the experiments showed that growth and nutrition were greatly affected by the light environment in which the animals lived. The effects produced by a given environment varied with the color or breed of the animal and appeared to be out of proportion to the differences in the intensity of the light or the energy represented. In a series of experiments dealing with the influence of light environment on normal rabbits, the growth of hair over shaved areas was used as an index of functional activity. The conditions compared were exposure to neon light, complete exclusion of light and exposure to diffuse, filtered sunlight of varying intensity. It was found that prolonged existence under these conditions affected the proliferative activity of hair follicles in a manner and to an extent comparable with the effects produced by the same environmental conditions on the growth and nutrition of the animals themselves.

[ARCH. PATH.]

THE EFFECT OF LIGHT ON BLOOD AND TISSUE CELLS. W. R. EARLE, J. Exper. Med. **48**:667 and 683, 1928.

Observations were made on hanging drops of blood obtained from veins in the ears of rabbits and exposed to irradiation. It was found that the red cells began to swell after from fifteen to thirty minutes, and then lost their hemoglobin, sometimes gradually, sometimes with explosive rapidity, hemolysis being complete at the end of from 90 to 110 minutes. Some cells also showed coagulation. In blood diluted with Locke's solution, the cells became hemolyzed one at a time instead of all at once. Hemolysis occurred at the same rate with white light and with light from each of the following spectral zones: (*a*) from 430 to 550 microns, infra-red; (*b*) from 475 to 630 and 690 microns, infra-red, and (*c*) 600 microns, infra-red. Washed cells underwent the same process of degeneration. The presence of air was apparently necessary, since in flat preparations from which air was excluded, degeneration did not take place. Changes in the white cells became evident only when hemolysis of the erythrocytes was complete, suggesting that substances liberated from the latter might be responsible for the degeneration of the former.

In the presence of autogenous red cells, fibroblasts from the hearts of embryo chicks also underwent degeneration when exposed to light, in the course of from three to four hours. The cells showed first an increase in the refractive index, followed by massive formation of vacuoles and sometimes by coagulation. The same wave length zones were active as in the case of the red cells, but the rate of degeneration varied markedly with light from the different zones, being slower through the blue or red filters and more rapid through the green filter. The presence of red cells was apparently necessary for the reaction, as in their absence only slight degeneration could be found even after from twelve to twenty-four hours.

B. R. LOVETT.

BIOLOGIC AND SEROLOGIC STUDIES OF STREPTOCOCCUS CARDIOARTHRITIS. WILLIAM A. KREIDLER, J. Infect. Dis. **43**:415, 1928.

The 107 strains of *Streptococcus cardio-arthritidis* studied exhibited a marked uniformity in their biologic reactions. All fermented dextrose, sucrose, inulin, salicin and raffinose; none fermented mannitol. Twenty-one strains (19.6 per cent) failed to ferment lactose and failed to produce acid in milk. None liquefied gelatin or produced indol.

Antigens prepared from each of the strains were agglutinated by a monovalent antiserum of *S. cardio-arthritidis* in dilutions high enough to indicate that these strains fall into a definite serologic group and that group agglutinins play but a small part in the results obtained. When the foregoing facts are considered, there seems to be reason for the belief that these micro-organisms biologically and serologically form a compact species of streptococci. The failure of some of the strains to ferment lactose and the difference in the agglutinability of the strains suggest that there may exist, within the species, immunologic subtypes of *Streptococcus cardio-arthritidis.*

[ARCH. PATH.]

DESTRUCTION OF DIPHTHERIA TOXIN BY BACTERIA. C. N. STARK, J. M. SHERMAN and PAULINE STARK, J. Infect. Dis. **43**:569, 1928.

It has been shown that several bacteria have the power to destroy diphtheria toxin when grown in its presence. The data reported show this to be true of *Bacterium coli, Bacillus cereus, Proteus vulgaris, Pseudomonas pyocyaneus* and *Clostridium sporogenes.* Especially active destruction was caused by *Clostridium sporogenes.*

[ARCH. PATH.]

BRILLIANT-GREEN ENRICHMENT METHODS IN THE EXAMINATION OF FECES FOR ORGANISMS OF THE ENTERIC GROUP. RUTH GILBERT and MARION COLEMAN, J. Infect. Dis. **44**:21, 1929.

This study would indicate that, for specimens which may be in transit twenty-four hours or more during submission to a laboratory, presentation in 30 per cent glycerol solution followed on receipt by inoculation of six plates of differential mediums would be a slightly better procedure for the isolation of *B. typhosus* than the Havens method. The preparation of the brilliant-green bile solution requires careful standardization, and irregularities may follow its use if its preparation is not adequately supervised. The use of either the Rakieten and Rettger or the Havens enrichment method in addition to the routine procedure of the New York State Laboratories would furnish a slightly higher percentage of successful isolations. Regardless of the method used, the submission of a series of specimens from each individual would seem to provide the best opportunity for the detection of typhoid carriers.

[ARCH. PATH.]

SOME PROPERTIES OF THE SEPARATED ACTIVE PRINCIPLES OF THE PITUITARY (POSTERIOR LOBE). J. H. GADDUM, J. Physiol. **65**:434 (Aug.) 1928.

Gaddum has presented the results of investigations on the supposedly purified preparations "vasopressin" and "oxytocin" recently isolated from the posterior lobe of the pituitary gland by Kamm, Aldrich, Grote, Rowe and Bugbee, and prepared by Parke, Davis and Co. He found that vasopressin contains 25 international standard units per cubic centimeter and oxytocin less than 1 unit per cubic centimeter. The rise in blood pressure produced by large doses of oxytocin was more prolonged than that due to small doses of vasopressin. One cubic centimeter of oxytocin contains from 12 to 15 units of oxytocic activity. Vasopressin contains less than 1 unit per cubic centimeter.

The diuretic action is produced by much smaller doses of vagopressin than of oxytocin. The diuretic effect of large doses of oxytocin on a cat under ether was, like the pressor effect, more prolonged than that of small doses of vasopressin.

Vasopressin did not show a depressor effect on a cat, even when given in repeated doses. One cubic centimeter of oxytocin (containing 12 units) did not show a depressor effect when given with soda. On the other hand, when 12 units of untreated oxytocin solution were injected into a cat in which the blood vessels were still in high tonus as the result of several large doses of vasopressin, a definite fall of blood pressure occurred. The effect is possibly analogous to the depressor action of pituitary preparations on the fowl. It has been investigated by Hagben who showed that the substance producing it is present in the pars neuralis and, to a less extent, in the pars intermedia, but not in other tissues. He also showed that it is destroyed by treatment with sodium hydroxide, and is accordingly not histamine. Gaddum found that a fall of arterial blood pressure was produced in a fowl under ether by large doses of vasopressin and of oxytocin, and also that oxytocin was active in much smaller doses than vasopressin. These two depressor actions, on the cat and on the fowl, are the only two actions, apart from that on the uterus, which have been found to be produced by smaller doses of oxytocin than of vasopressin, and it is possible that they are both due to the oxytocic principle itself. This would accord well with the fact that such effects are produced by Abel's purified preparations, in which the oxytocic titer appears to be extraordinarily high.

It was found that, though both preparations produced shortening of an isolated loop of the rabbit's intestine, and an increase in peristalsis, vasopressin produced these effects in smaller doses than oxytocin. This effect is rather irregular. The colon appeared to be more sensitive than the ileum, and the ileum more than the jejunum. Previous work on this question is summarized in a paper by MacDonald, who found that pituitary preparations had little if any specific effect on the isolated intestine of the cat. Gaddum confirmed this observation.

The activity of the different preparations on frog's melanophores does not bear a constant proportion either to their pressor or to their oxytocic activity. The dilator action on the melanophores is probably due to a separate substance, although some of this is present in vasopressin.

Gaddum concludes that "oxytocin" has, in addition to its action on the uterus, a depressor action on the fowl, and, in certain circumstances, on the cat. "Vasopressin" has, in addition to its effects on the blood pressure and on the kidney, a specific stimulant action on the bowel of a rabbit and a dilator action on the melanophores of the frog. The latter effect is apparently due to a different principle, so that vasopressin is not as yet a physiologically pure preparation.

ALPERS, Philadelphia.

GENERALIZED VACCINIA IN RABBITS WITH INTERNAL LESIONS. S. R. DOUGLAS, WILSON SMITH and L. R. W. PRICE, J. Path. & Bact. **32**:99, 1929.

A condition of experimental generalized vaccinia in rabbits is described which closely resembles human smallpox of the alastrim type. In this generalized disease almost every tissue of the body may be affected with the production of macroscopic lesions; no injury or irritation is necessary. The internal viscera most commonly affected are the lungs, liver, spleen, adrenal glands and the organs of reproduction. The kidneys are exceptional in that they have never shown generalized lesions. The mesodermic origin of an organ does not indicate a nonsusceptibility to vaccinia. A strain of testicular passage virus was obtained which was highly infective when introduced by intraperitoneal inoculation; it produced a vaccinial peritonitis and gave rise to pathologic lesions in organs hitherto thought to be nonsusceptible, for instance, in the uterus, bladder, peritoneum and muscle. Vaccinia virus may remain latent in the tissues of an immune animal for a long period (up to at least forty-one days) after infection. Virus was recovered from the blood of an animal six days after infection. Infectivity of the blood is irregular and appears to have no correlation with the time incidence of generalization. Vaccinal infection caused abortion in three pregnant rabbits in all of which there was particular localization of lesions in the uterus. Both placenta and fetus contained virus.

[ARCH. PATH.]

THE PROTECTIVE ACTION OF SERUM AGAINST HEMOLYSIN IN DIPHTHERIA. J. GORDON and J. SCIENCE, Quart. J. Med. **21**:345, 1928.

In diphtheria the protective power of the serum against a hemolysin is markedly diminished, this protective power returning in simple uncomplicated cases by the end of the third week. In most cases of paralysis, the diminished protective power lasts for a considerable time. In a few cases of paralysis there will be no interference with protective power of the serum. In fatal cases there is a marked loss of the protective power. The protection of the serum against hemolysin should be estimated early in the disease as an indication of the amount of toxin present in the blood, in order to find some index to the amount of antitoxin to be injected and at various periods of the disease in order to assess the prognosis and the possible development of paralysis.

N. ENZER.

COMPLEMENT FIXATION IN CUTANEOUS TUBERCULOSIS (BESREDKA'S METHOD). LORTAT-JACOB, BIDAULT, LEGRAIN and URBAN, Ann. de dermat. et syph. **9**:841 (Oct.) 1928.

On the assumption that light could be thrown on the question of the cutaneous tuberculoses and the tuberculids, the authors investigated a series of cases with the complement-fixation test. This test is of the same significance in tuberculosis of the skin as it is in visceral manifestations of the disease. It was found that the test was positive in about 90 per cent of the cases of tuberculids. For the authors, this group comprises papulonecrotic tuberculid, Bazin's disease, lupus erythematosus and lupus pernio. In frank tuberculosis cutaneous, the fixation test gave a smaller percentage of positive reactions than in the tuberculids and more frequently positive in the ulcerative than in the nonulcerative forms. Of the doubtful tuberculids (granuloma annulare, pityriasis rubra pilaris, erythema nodosum, angiokeratoma, supramalleolar erythrocyanosis) the results obtained were indefinite, and no deductions could be drawn. But for lupus pernio and lupus erythematosus, the results obtained support the argument of the partisans of a tuberculous pathogenesis.

The large proportion of negative reactions in frank skin tuberculosis is discussed, and by the authors considered paradoxic: the result of an immunologic (allergic) play.

In a short appended note the authors mention favorable effects in cutaneous tuberculosis and in tuberculids with the methyl antigen of Boquet and Negre.

[ARCH. DERMAT. & SYPH.]

RESEARCHES ON SERUM ANAPHYLAXIS. E. SUAREZ, Ann. de l'Inst. Pasteur **42**:877, 1928.

Euglobulin, pseudoglobulin and serum albumin act as different antigens; each sensitizes specifically and is toxic for animals sensitized with whole serum and with corresponding antigen. The specificity of the neighboring fractions (pseudoglobulin-euglobulin, pseudoglobulin-serum albumin) is such that animals sensitized with one fraction resist from ten to fifteen lethal doses of the other fraction. The specificity of the less related fractions (euglobulin-serum albumin) is such that animals sensitized with one resist from fifteen to eighty lethal doses of the other. These antigens sensitize after different periods of incubation. The minimum (nine to twelve days) proper for serum anaphylaxis is reduced in euglobulin anaphylaxis to from three to six days; it is from twelve to fourteen days in serum-albumin anaphylaxis, and from eight to ten days in pseudoglobulin anaphylaxis.

[ARCH. PATH.]

CHOLESTEROL CONTENT OF THE BLOOD IN HYDROLABILE CHILDREN. F. HAUSTEIN, Arch. f. Kinderh. **86**:33 (Dec. 28) 1928.

Haustein found the blood cholesterol in eight hydrolabile children to vary from 120 to 135 mg. per hundred cubic centimeters in the following degree: In

intoxication and pyodermitis associated with myxedema, it was 120 mg.; in intoxication with erythrodermitis following a nutritional disturbance, 126 mg.; in goat's milk anemia with pyelitis and dyspepsia, 130 mg.; in congenital syphilis, 133 mg.; in chronic dyspepsia with grippal infection 135 mg., in a case of dysentery, 135 mg.

SANFORD, Chicago.

THE SPECIFIC DYNAMIC ACTION AND THE SYMPATHETIC NERVOUS SYSTEM. S. EDERER and J. WALLERSTEIN, Biochem. Ztschr. **206**:334 (March) 1929.

The authors found that the specific dynamic action of protein and carbohydrate was inhibited when the sympathetic nerves were paralyzed by the administration of ergotamine. The authors assert that the specific dynamic action is dependent on a sympathetic reflex initiated in the intestinal mucosa.

BRAHDY, New York.

THE DEMONSTRATION OF VACCINE VIRUS IN THE BLOOD AFTER CUTANEOUS INOCULATION. E. GILDERMEISTER and GEORG HEUER, Centralbl. f. Bakteriol. **105**:86, 1928.

The cutaneous injection of variola vaccine into rabbits was followed by its appearance in the blood within as short a time as two hours; it remained there for several days, as demonstrated by the method of Calmette and Guerin. The injection of a suspension of Pelikan ink (25 cc.) had no influence, the authors thereby concluding that blockading the reticulo-endothelial system has no influence on the demonstration of the vaccine virus in the blood stream.

PAUL R. CANNON.

BLOOD PROTEIN IN CHILDHOOD. HEINRICH SUSSMANN, Deutsche med. Wchnschr. **54**:23, 1928.

The author states that there are no reliable methods for determining the protein content of the blood. Even if there were, the normal physiologic variation would make any clinical evaluation difficult. The only definite change which is known to occur in disease, is the increase in fibrin and globulin at the expense of the albumin in inflammatory conditions.

HEMOGLOBIN RESISTANCE AS AN INDEX OF THE AGE OF NURSLINGS AND PREMATURELY BORN. H. BISCHOFF, Deutsche Ztschr. f. d. ges. gerichtl. Med. **11**:340, 1928.

When all are used together, the many conditions on which the duration of gestation of new-born infants is estimated are fairly reliable. Among these are the weight, length of the nails, consistency of the skin and size of certain foci of ossification. But these have little value for determining the age some weeks or months after birth at term, although by some investigators considerable reliance is placed on the length and size of certain bones. Bischoff has used the resistance of the hemoglobin to alkalis not only to ascertain the age of prematurely born infants, but also to decide during the first year of their life the time of conception of prematurely born infants, if the date of their birth is known. These are matters of importance in connection with foundlings, illegitimacy and questions of parenthood. The method was described by Korber in 1866 and has been somewhat modified since. Its details are too involved to be given here. The age is learned to within a few weeks. The tests were made by Bischoff on the blood of 100 nurslings and thirty-eight prematurely born infants. Fetal hemoglobin is more resistant to the action of alkali than in hemoglobin in adults, and that of a prematurely born infant is also more resistant than is the hemoglobin of an infant of the same age born at term. It is of considerable interest that these tests can be employed with the hemoglobin of decomposed or dried blood even though it has been kept for several years. The tests have been useful in demonstrating birth at term of infants already dwarfed.

E. R. LE COUNT.

THE ASH CONTENT OF THE GROWING ORGANISM. HUGO MEYER, Habitationsschrift, 1929.

Experiments performed on healthy young rats showed that on a calcium enriched diet the retention of calcium increased until it was 20 per cent above normal on the fifth day. A further increase did not take place; in fact, after this time, the calcium content of these rats approached that of the control group. The increase in calcium retention in the rats fed on the enriched diet is comparable to that seen in the bottle-fed infant contrasted with the breast-fed child.

The increase in the calcium of the bones was less than the total increase in calcium, indicating either that some of the calcium was retained in the soft tissues or that the total amount of bony substance was increased. Older rats did not show any calcium retention regardless of the enrichment of the diet.

LESLIE, Evanston.

SOURCES OF ERROR IN DIFFERENTIAL COUNT OF WHITE CORPUSCLES IN STAINED BLOOD SMEARS. C. GYLLENSWÄRD, Acta paediat. **8**:1 (March 6) 1929.

Practical considerations such as convenience and expense have made the slide smear method for differential counts more popular than the cover-slip technic. Though the film preparation is satisfactory from a technical point of view, there are still several sources of error in the differential count to be made from it which have hitherto been ignored or have been investigated on inadequate material.

When a slide smear is prepared in the usual way, by placing a drop of blood on the left-hand side of the slide, allowing it to lengthen out by capillarity along the edge of a superimposed slide and then drawing it out to the right, one can show by counting different portions of the preparation: (1) that leukocytes of all forms tend to concentrate along the upper and lower margins of the smear and also in the elongated tongues at the right where the smear comes to an end, and (2) that this tendency to unequal distribution varies according to the size of the various types of leukocyte, being least in the case of lymphocytes and greatest in the case of monocytes. It is thus easy to show how, in a single preparation, a count made from the middle part of the film may give a relative lymphocytosis while one made from the edges may show a neutrophilic leukocytosis. For clinical purposes it is obviously out of the question to count every white cell in a single smear, but the author asserts that a representative result may be obtained by counting along vertical lines which cross the entire width of the smear perpendicular to the long axis of the slide and which therefore, by including both the inner part and the upper and lower edges, effectively neutralize the unequal distribution of cells. By making differential counts on ten groups of 100 cells in each of 150 stained slides, he obtained sufficient material for a statistical treatment of his results and presents figures showing the accuracy represented by a count based on 100, 200 or more cells in a single smear.

There is a limit, however, to the degree of refinement with which one may wisely pursue the differential count in a single smear because of the question whether this smear accurately represents the patient's blood as a whole. To investigate this source of error, the author compared films from the fifth and sixth drops flowing spontaneously from the needle wound. Naturally, one cannot say that either one or the other of two such smears is the more representative of the patient's blood; yet differences in composition were found of such magnitude that the author advises against carrying the differential count in a single smear through more than a total of 300 cells. These differences likewise demonstrate the futility of claiming that either the slide method or the cover-slip method is more accurate than the other, and the argument between them boils down to one of convenience. An approach to an accurate count is to be obtained by counting two or three hundred cells in each of several smears, rather than one or two thousand cells in a single smear.

MCINTOSH, Baltimore.

THE ETIOLOGY AND PATHOLOGIC ANATOMY OF REACTIONS AFTER TRANSFUSION OF BLOOD. ARVID LINDAU, Acta path. et microbiol. Scandinav. **5**:382, 1928.

This article gives a review of the literature on unfavorable reactions following transfusion with reports of three illustrative cases studied by the author. The severe reactions depend on the transfusion of incompatible blood followed by hemolysis. The principal lesions develop in the kidneys and liver, and in certain cases also in the intestine. The lesions in the kidneys and the necroses in the liver are microscopically characteristic.

[ARCH. PATH.]

Nutrition

STUDIES ON THE COMPOSITION OF HUMAN MILK. M. BELL, J. Biol. Chem. **80**:239, 1928.

Consecutive analyses of the breast milk of eighty-eight normal women are reported. The tables presented indicate that the ash and protein content of the milk steadily decrease during the first few days post partum, while the fat and lactose content gradually increase. The influence of supplementary feedings of carbohydrate and fat on the composition and volume of the milk is discussed.

ARTHUR LOCKE.

THE ELIMINATION OF NICOTINE IN MILK. R. A. HATCHER and H. CROSBY, J. Pharmacol. & Exper. Therap. **33**:1, 1927.

Characteristic physiologic responses are obtained when nicotine in as small a ratio as 1 : 500,000 is injected into the lymph sacs of frogs. Still smaller quantities may be recognized by the odor when concentrated and pure extracts are made alkaline. It was found that lactation was markedly lessened or altogether checked in cows and cats by nicotine; although abundant, at first, in a primipara accustomed to smoking from twenty to twenty-five cigarets a day, the flow of milk quickly diminished. The smoking of seven cigarets in two hours caused a marked subsidence. In purified extracts of the milk, nicotine was easily demonstrated. The effect on nurslings has not been investigated.

[ARCH. PATH.]

THE MILK FEEDING OF CHILDREN. E. B. STERLING, Pub. Health Rep. **44**:957 (April 19) 1929.

The author gives a résumé of the various demonstrations of breast feeding in the various states, and the resulting decrease in infant mortality. In artificial feeding, cow's milk is recommended in the majority of cases. Dried milk is a good substitute when cow's milk is not available. Lactic acid milk is discussed, both that made with the whole milk and that made with evaporated milk. The chief drawback to this type of feeding is the difficulty of preparation. The author thinks that the sale of raw goat's milk should be prohibited.

SANFORD, Chicago.

STUDIES ON SCURVY. ARTHUR W. MEYER and LEWIS MCCORMICK, Stanford University Press, 1928, pp. 1071.

THE SYMPTOMATOLOGY AND GROSS MORPHOLOGY OF EXPERIMENTAL SCURVY IN THE GUINEA-PIG. ARTHUR W. MEYER.

As far as the gross lesions regarded as diagnostic of experimental scurvy in the guinea-pig are concerned, the author adds little except that the presence of fatty degeneration in the liver and absorption on the roots of the molar teeth, with the possibility of depressing the posterior or all of the molars, are constant morphologic signs. The extent of depression that is possible always is greatest in the last molars and decreases from back forward. Outwardly evident lesions in the bones and joints usually are absent in the mature guinea-pig, and such

animals may show evident signs of pain without the presence of swollen or tender joints and without hemorrhage in the extremities. They also may be active and apparently unaffected and yet have extensive hemorrhages and may have suffered considerable absorption on the roots of the molars and in the alveoli. Some subcutaneous and muscular hemorrhage is almost always present somewhere at the time of autopsy, and duodenal, cecal and vesical (urinary) and paravesical hemorrhages are common. The stomach and, in fact, the entire intestinal canal, usually contains little food, and I have come to regard the lack of appetite and interest in food and also the lessened activity among the earliest signs of the existence of the scorbutic condition. An entire lack of interest in food always was an absolute indication of death within a few days no matter how well the animal seemed or how active it was. Increasing inactivity and weakness and increased loss in weight and appetite usually enabled one to forecast the approximate time of death except for the advent of sudden complications. The new observations on the gross pathologic condition of experimental scurvy in guinea-pigs here reported are: the highly nervous condition of some of the animals; the recovery of health of young pigs after a condition of complete helplessness in the posterior half of the body; the occurrence of permanent locomotor disabilities; shortening of the roots of the teeth by absorption so that the molars can be depressed below the level of the gums; the occurrence of pronounced gaseous distention of the stomach in some animals, and pseudopneumonic lesions in the lungs of others; fatty change, even to whiteness, especially of the liver, to a lesser degree of the suprarenals, and microscopically also in other organs, as will appear in part II; necrotic areas in both liver and suprarenals; degenerative changes in and fibrosis of the costal cartilages even in regions remote from the costochondral junctions.

THE MINUTE MORPHOLOGY OF EXPERIMENTAL SCURVY IN THE GUINEA-PIG. ARTHUR W. MEYER.

Hemorrhages were noted rarely in the skin, almost universally somewhere in the subcutaneous tissues, commonly in the muscles, the urinary bladder, the periostea, the periodontia, many glandular organs, and the lungs, stomach and intestine. They were also seen in the gallbladder, the brain, spinal cord, posterior root ganglions and the nerve trunks. Intragingival and intra-articular hemorrhages were not observed. The marked fatty infiltration and degeneration evident grossly in the liver and sometimes also in the kidney were found present microscopically in the kidney, the suprarenal, and even in the lung and the peribronchial cartilages, the pancreas, some skeletal muscles, and the walls of a blood vessel. Degenerative changes other than fatty changes, resulting in the complete loss of substance, were observed in the cartilages, bones, teeth, muscles, many glandular organs and also in the central, the peripheral and the sympathetic nervous systems. This widely distributed liquefaction of the cytoplasm and cell walls results in destruction of cartilage cells and of the cartilaginous matrix, at least in the costal cartilages; in the detachment of the periostea and periodontia; in reduction in caliber of the bones, and in both the caliber and the length of the implanted portions of the teeth. It may effect not only the separation of ununited epiphyses and loosening of the teeth, but the complete destruction of the parenchyma of some areas in the glandular and other organs, in desquamation of the mucosa and of renal epithelium, and in complete disintegration of the walls of blood vessels. In addition to the fatty and lytic changes, coagulative changes, such as extreme waxy degeneration in the muscles, were also noted in glandular and nervous tissues. The only proliferative changes noted occurred in the costal cartilages and concerned an increase in caliber at the region of the costochondral junctions and an invasion of connective tissue into areas of degeneration. Necrotic areas on the surface and in the substance of the liver were occasionally observed, but may be wholly unrelated to scurvy. Vacuolation was common in many organs, and fenestration up to a marked degree was observed, especially in muscle, bone marrow, the pulp of the teeth, and also in the cord and brain.

SOME CHARACTERISTICS OF THE BLOOD OF THE GUINEA-PIG IN EXPERIMENTAL SCURVY. LEWIS M. MCCORMICK.

Definite cytologic changes occurred in the blood of guinea-pigs with experimental scurvy. These changes became evident after the pigs were on the author's scorbutic diet for ten days. They consist of a decrease in red blood cells, hemoglobin and color index, an "apparent" decrease in fragility, a relative decrease in the number of lymphocytes and an absolute increase in polymorphonuclears, and an increase in reticulated and nucleated red blood cells and leukocytes. The eosinophil, basophil, monocyte and transitional cell counts were not considered characteristic of scurvy.

[ARCH. PATH.]

"FRUIT POISONING:" AN INVESTIGATION OF ITS ETIOLOGY, SYMPTOMATOLOGY AND PATHOLOGY, WITH SUGGESTIONS AS TO TREATMENT. L. B. KINGERY, Warthin Ann. Vol., 1927, p. 49.

An occupational dermatosis, known among cannery workers as "fruit poisoning," has existed in certain portions of the Northwest for at least five or six years. The incidence is estimated to be as high as 33.3 per cent of those employed as handlers of fruit. The symptomatology consists of marked paronychia, characterized by inflammatory reaction, pain and loss of one or more finger nails. In addition, maceration, vesiculation and fissuring between the interdigital aspects of the fingers is frequently found, together with occasional patches of erythematovesicular dermatitis on the hands and forearms. The course of the disease is acute during the pear season.

Cultures from several patients have uniformly revealed pure cultures of a yeastlike organism. Inoculations in animals and in man with organisms thus obtained result in a clinical picture practically identical with known mycelial infections of the skin. It would seem that so-called "fruit poisoning" may be properly classified with the dermatomycoses.

WALTER M. SIMPSON.

THE EFFECT OF ANTENATAL AND POSTNATAL DIET ON THE STRUCTURE OF THE TEETH AND THE INCIDENCE OF DENTAL CARIES. MAY MELLANBY, Edinburgh M. J. **36**:25 (March) 1929.

In this address before the obstetric society of Edinburgh, Mrs. Mellanby reviews the conclusions that she has formed from the work of herself and her husband, Dr. E. Mellanby, during the past fifteen years. She presents a table showing the results of the surface and histologic examinations of 1,036 human deciduous teeth, disclosing that only 14 per cent were perfect in construction. In explanation, she experimented extensively on puppies as the most suitable animal from which to draw conclusions as to similar conditions in man. She has, however, conducted dietary experiments on rabbits and rats and, on a small scale, in human beings. She discusses the factors assisting in the calcification of the teeth, namely, vitamin D, the presence of calcium and phosphorus in the diet, and the effect of exposure of the skin or of certain foodstuffs to ultraviolet radiations. Employment of these factors results in the development of perfect teeth. Another interesting observation brought out by the work of the Mellanbys is that of the interference of certain foods with calcification of teeth. Cereals were found to be anticalcifying in their effect, oatmeal being the most powerful in this line.

From the experimental work, it became clear that the mother's diet during pregnancy and lactation exerted an influence on the degree of development of teeth in her offspring. Deficient diets caused the pregnant animal to abort, or the offspring, if born alive, were reared with difficulty. The deciduous teeth of the progeny were usually defective in structure, while puppies whose mother was given an abundance of vitamin D had teeth of normal structure. Puppies of a mother whose diet had been deficient in vitamins had imperfectly calcified deciduous teeth. There is less chance for hindrance of calcification before birth than for calcification which proceeds during the period of nursing or artificial feeding of

the infant. The author concludes that an abundance of vitamin D should be given to the pregnant mother not only for her sake but for that of the child. Among many useful foods, the diet should include milk, egg yolk, animal fat and cod liver oil. (A complete review of the subject by Mrs. Mellanby will be found in *Physiol. Rev.* **8**:545, 1928 [Abstr.].)

NEFF, Kansas City.

THE ASSOCIATION OF BOWEL DISEASE WITH VITAMIN C DEFICIENCY. F. P. MACKIE and G. D. CHITRE, Indian J. M. Research **16**:77, 1928.

Monkeys on a diet deficient in or lacking vitamin C become debilitated and anemic, lose weight rapidly and generally suffer from a terminal fatal dysentery. Definite signs of scurvy appear in most of the animals. This scorbutic condition can be checked by the administration of orange juice or by a return to a normal dietary, provided it is not advanced. When once the scorbutic condition is well established, this treatment cannot be depended on to save the animals' lives. The postmortem signs are most marked in the large intestine, which shows a succession of changes suggestive of local poisoning. These signs vary from local congestion and thickening of the mucous membrane to a condition indistinguishable from ulcerating and sloughing dysentery. The morbid histology suggests degenerative changes due to the action of a toxin, to which inflammatory changes are added secondarily. Specific excitants of dysentery such as amebas or dysentery bacilli are not found in the large majority of cases. The commoner fecal flora, in some cases, are found to have invaded the living tissues of the bowel wall, and this suggests that the toxic changes observed are the effect of such bacteria acting on tissues devitalized by the ill-balanced dietary. These changes appeared in the alimentary canal in all animals kept on a diet deficient in vitamin C whether given infective sprue material or not. Monilia were not found to have invaded the diseased areas, nor can the changes be attributed to their action. A defective dietary by itself powerfully predisposes to bowel derangements and acts probably by reducing the natural resistance of the intestinal epithelium to the invasion of bacteria or their toxins.

[ARCH. PATH.]

THE EFFECT OF ULTRAVIOLET LIGHT ON THE BODY AND GROWTH OF THE CHILD. M. SANDER, Arch. f. Kinderh. **86**:8 (Dec. 28) 1928.

The eleventh article of this series deals with the amount of hemolysis permitted by the different types of glass presumably permeable to ulraviolet rays. When the total hemolyzing time of blood exposed to ultraviolet light was given as 100 per cent, the same strength of exposure through 2 mm. quartz glass varied from 80 to 93 per cent. In the same length of time, various types of commercial glass gave periods of hemolysis varying from 7 to 40 per cent.

SANFORD, Chicago.

EXPERIMENTS IN LOW CARBOHYDRATE FEEDING. P. GYÖRGY and H. KELLER, Biochem. Ztschr. **206**:120 (Feb.) 1929.

The authors compared the growth of young rats fed a carbohydrate-free diet with the growth of rats fed a balanced diet. The animals on the carbohydrate-free diet grew practically as well as the control animals. The blood sugar remained normal. The authors assert that the high carbohydrate requirement of the growing organism can be supplied indirectly by fat and protein.

BRAHDY, New York.

MODERN COD LIVER OIL THERAPY. JOHANNES JOCHIMS, München. med. Wchnschr. **43**:1832, 1928.

This study is concerned with the use of a preparation of cod liver oil combined with cocoa-malt put out by a German firm. Ten cubic centimeters given three times a day cured patients with florid rickets in from three to eight weeks

(checked by the x-rays). The author asserts that there is an advantage in using a preparation containing vitamin D, which retains the food value of cod liver oil yet does not have its objectionable taste.

LESLIE, Evanston.

BREAST-FEEDING AND THE LIVING CONDITIONS OF MOTHERS. M. GRANESKI, Opieka nod Dzieckiem **6**:187 (May-June) 1928.

A great propaganda is launched by different Polish organizations to teach mothers that breast milk is the best food for infants. Because of economic conditions in the country a mother in the poorer classes has to work in a factory to help support the family; milk under such conditions cannot be the ideal food for the infant. In order that the milk may be the ideal food, the mother must receive proper food during pregnancy and lactation.

Failure to nurse the infants is based on: (1) social position and (2) economic position. In factories where mothers are compelled to work during lactation, a nursery is organized where babies are left and the mother can come and nurse the baby regularly; also when the mothers are poor, proper food is supplied by charitable organizations.

KRUPINSKI, Chicago.

INFANTILE BERIBERI WITH SYMPTOMS OF HUMAN MILK INTOXICATION. T. HACHIYA, J. Pediat. (Tokyo), Jan. 20, 1929, no. 344, p. 174.

The author reports three cases of breast-fed infants, from 10 to 12 months of age, all with vomiting, muscular weakness, loss of appetite and more or less marked strabismus with loss of eyesight. In one case, the mother had the cardiac type of beriberi, but the others had normal health. Treatment consisted of the hypodermic and oral administration of vitamin B. Two of these infants died, while the third made a complete recovery. The most unfavorable symptoms are loss of eyesight and diarrhea.

KATO, Los Angeles.

Prenatal Conditions

THE PATHOLOGIC AND CLINICAL SIGNIFICANCE OF CONGENITAL ONE-SIDED DEFECT OF THE KIDNEY, WITH THE PRESENTATION OF THREE NEW CASES OF AGENESIA AND ONE OF APLASIA. C. H. FORTUNE, Ann. Int. Med. **1**:377, 1927.

Fortune adds 3 cases of unilateral agenesia of the kidney to the 419 instances which he collected from the literature. The ureter on the affected side was said to be absent in 54 per cent of the cases and present in 10 per cent, while the absence of the renal vessels was noted in 100 cases. In 46 cases, the suprarenal gland was reported absent. Associated genital malformations, usually due to arrested development of derivatives of the müllerian or wolffian duct, occurred in 70 per cent of the female and 22 per cent of the male patients studied. A single existing kidney is more likely than two normal kidneys to become diseased. A case is reported of left renal aplasia, associated with the following multiple anomalies: cheilognathopalatoschisis, Meckel's diverticulum, multiple diverticula of the colon, malformations of the ear and stenosis of the aortic isthmus.

CONGENITAL ATRESIA OF AORTIC RING. N. PHILPOTT, Ann. Int. Med. **2**:422, 1928.

Philpott describes the autopsy observations in the case of an infant who lived sixty-two hours after birth. On the day after delivery, cyanosis appeared and deepened progressively until death occurred. The administration of oxygen was without effect. There was no mitral opening. A direct communication between left and right auricles was established by means of a widely patent foramen ovale. There was complete atresia of the aortic ring. The ductus arteriosus was widely patent.

WALTER M. SIMPSON.

ON THE INHERITANCE OF AGGLUTINOGENS OF HUMAN BLOOD DEMONSTRABLE BY IMMUNE AGGLUTININS. K. LANDSTEINER and PHILIP LEVINE, J. Exper. Med. **48**:731, 1928.

The heredity of two agglutinable structures demonstrable by immune agglutinins was studied in 166 families. From the data collected, it is evident that one deals with a case of mendelian inheritance. The main result of the studies is the demonstration that it is feasible to investigate the heredity of serologic structures of human blood other than the group agglutinogens. Irrespective of the ultimate theory it seems probable that the properties M and N do not appear in the offspring when they are absent in both parents — a conclusion substantiated by the examination of ten families with forty-six children. These observations offer the prospect of forensic application to cases of disputed paternity and, in our opinion, a correct decision could already be given, at least with great probability, provided the reagents are available and the method properly applied. Of course, further work is needed before the test can be adopted as a routine procedure.

[ARCH. PATH.]

THE PROBLEM OF THE PREMATURE INFANT. EDMUND H. HUBNER, M. Clin. North America **12**:795 (Nov.) 1928.

Measures essential to the successful care of premature infants are: maintenance of a moist, equable temperature, prevention of dehydration, protection from infection, and breast milk. The first requirement is met by a simple form of home-made incubator supplying moist air, which is fully described in this paper. Dehydration is prevented by moistening the air which surrounds the infant, by hypodermoclysis of a 5 per cent solution of dextrose in normal physiologic solution of sodium chloride and by oiling the infants instead of washing them. Infection is guarded against by proper nursing and by avoidance of handling by other persons than a special nurse. In obtaining a sufficient supply of breast milk, the electric breast pump has proved not only a great convenience, but also a source of comfort to mothers with engorged and painful breasts.

SMITH, Ogden, Utah.

CRANIOSYNOSTOSIS (OXYCEPHALY AND RELATED DISORDERS). H. K. FABER, Warthin Ann. Vol, 1927, p. 585.

Faber includes as varieties under the generic term "craniosynostosis" such cranial deformities as oxycephaly (steeple-skull), turricephaly (tower-skull), scaphocephaly, trigonocephaly and phagiocephaly. All have their origin in pathologic synostosis of two or more bones of the calvarium, and are associated in a certain proportion of cases with deformities resulting from synostosis or fusion of adjoining bones in other parts of the body. The anterior and superior portions of the skull (coronal and sagittal sutures) are most frequently involved.

The malformations are conditioned by two factors: first, interference with normal expansion and, second, compensatory overexpansion of unsynostosed regions to accommodate the growing brain. The mechanisms of the development of these deformities are discussed in detail.

The instances of craniosynostotic deformities in more than one generation of a given family are exceptional. More common are examples of their appearance in more than one member of the same generation.

The distinguishing feature in the diagnosis is that the cranial cavity, while deformed, is of normal volume. Visual defects are common and greatly influence the prognosis.

WALTER M. SIMPSON.

CONGENITAL ANEURYSM OF THE CEREBRAL ARTERIES. F. GREEN, Quart J. Med. **21**:419, 1928.

From 1922 to 1927 at St. Bartholomew's Hospital, London, nineteen bodies at autopsy presented basal cerebral aneurysms, and in seventeen death was due

to their rupture. Five of these were embolic and associated with malignant endocarditis; two were associated with extensive arteriosclerosis, and twelve were congenital. In three bodies two aneurysms were found, and in one three saccular dilatations were seen on various branches of the circle of Willis. The average age of death in the embolic type was 25 years, in the sclerotic type, 58 and in the congenital type, 43. The average age at death from lenticulostriate and pontile hemorrhage was 58 years. The three reports under consideration concerned: a single woman, aged 30, who lived for six weeks with leakage from a saccular aneurysm of the right middle cerebral artery; a married woman, aged 49, who died two days after the onset of bleeding from an aneurysm identical with the foregoing one, and a man, aged 21, who had suffered repeated attacks of headache and loss of consciousness. Death occurred in the last patient fifteen hours after the last attack, and at autopsy three aneurysms were found associated with coarctation of the aortic isthmus, a bicuspid aortic valve and fenestrated mitral cusps. Histologically, the essential changes in the aneurysm walls were atrophy and connective tissue replacement of the media occurring frequently at a single point in the circumference and associated with splitting of the elastic lamina and subendothelial hyperplasia of the intima.

GEORGE RUKSTINAT.

CONGENITAL STRUCTURAL ANOMALIES OF THE PULMONARY ARTERY. A. COSTA, Arch. di pat. et clin. med. **7**:329 (Sept.) 1928.

This study is based on histologic and micrometric examinations of pulmonary arteries (210 cases) in various decades of life and of both sexes. In each instance, the micrometric measurements of the single layers of the arterial wall and the histo-analysis were made in the lower third of the artery. Under normal conditions, the thickness of the media in children varies between 0.35 and 0.5 mm.; in the adolescent periods of life it reaches a thickness of from 0.6 to 0.650 mm., and in advancing age it measures between 0.7 and 0.85 mm. While the intimal layer is extremely thin (0.01 mm.) in the first years of life, it presents in adolescence a gradual enlargement, showing a thickness of from 0.015 to 0.02 mm. and in later decades, 0.03 mm. This progressive enlargement of the media is due to an increase in the density of the circulatory distributed elastic lamellae and to a further development of the muscle tissue. The gradual thickening of the intima occurs on account of the increasing density of the internal elastic membrane and the formation of a delicate subendothelial layer of connective tissue.

The structural malformations found were mainly of hypoplastic nature. Three definite types were observed: 1. Muscular hypoplasia affects the artery diffusely and is characterized by muscle tissue that is little developed or totally absent. The elastic apparatus, as well as the interstitial connective tissues, often appear hyperplastic. However, the muscular hypoplasia rarely occurs, without a concomitant hyperplasia of these two tissues. 2. In another type of musculo-elastic hypoplasia, not only are the muscular elements scarce, but also the structurally important, circularly-running elastic lamellae are extraordinarily thin. The interstitial connective tissue usually exhibits a diffuse hyperplasia. 3. The elastic hypoplasia is characterized by greatly hypoplastic elastic apparatus, while the muscular tissue reaches an otherwise moderate development. In hypoplastic conditions of the first and second types, the media may show a nearly normal thickness (0.75 mm. in persons from 30 to 40 years of age) due to hyperplastic processes of other tissues. In the second type, however, the media never achieves its normal size and the pulmonary artery then greatly resembles its early (from 1 to 5 years of age) forms during extra-uterine development. The intima does not exhibit any structural abnormalities in the aforementioned hypoplastic conditions of the media, except that the internal elastic membrane participates, more or less, in hyperplastic or hypoplastic processes of the media layer. These investigations do not confirm the observations of Orliansky in regard to hypoplasia of the cerebral arteries (Thèse de Genève, 1919).

In 14 per cent of all the cases examined post mortem, such structural anomalies of the pulmonary artery were observed. One could not establish any correlation between the described anomalies of the pulmonary wall and the development of atherosclerosis. In 90 per cent of the cases investigated there was a parallelism between the hypoplasia of the aorta and hypoplastic conditions of the pulmonary artery; in 16 per cent of the cases showing the latter condition, a chronic pulmonary tuberculosis was present.

E. L. MILOSLAVICH.

TWO CASES OF EXSTROPHY OF THE BLADDER. C. HERNANDEZ, Bol. Soc. Cubana de pediat. **3**:109 (March) 1929.

The first child was seen at 11 days of age. A roentgenogram of the injected ureters showed them to be normal. The second case was similar. The frequency of this malformation in Cuba is about 3 in 14,000. A plastic operation is advised as soon as the child's condition will warrant.

SANFORD, Chicago.

CONGENITAL TORTICOLLIS. GARRIDO LESTACHE, Pediatría españ., July, 1928, vol. 17.

Congenital torticollis must be differentiated from a torticollis due to suboccipital disease. The clinical symptoms are different. Careful roentgen examination of the cervical region of the vertebral column will reveal Pott's disease. There is considerable pain on pressure or movement in the region of the neck in this disorder and almost complete absence of it in congenital torticollis.

The author recommends simple open tenotomy rather than more complicated surgical procedures like those advocated by Mickulicz, Fordele and Wullstein. The correct postoperative mechanotherapeutic care of the patient is the most important part of the treatment.

SCHLUTZ, Minneapolis.

CONGENITAL LIPOMA OF THE FEMORAL VEIN. J. GANGLER, Virchows Arch. f. path. Anat. **265**:643, 1927.

A lipoma the size of an orange was removed from the femoral vein of a girl, 18 months of age. The vein ran through a groove in the mass, which was surrounded by a fibrous capsule everywhere except where there was contact with the vein. The point of origin appeared to be the adventitia of the vein. Since this tissue does not normally contain fat cells, the development of a lipoma from it is evidence for the theory of embryonic displacement of tissue rests as a cause of tumor development.

B. R. LOVETT.

A TUMOR-LIKE NODULE IN THE LATERAL WALL OF THE SPINAL CORD IN A HUMAN EMBRYO OF 16.5 CUBIC MILLIMETERS. ARTHUR BERGEL, Ztschr. d. d. ges. Neurol. u. Psychiat. **116**:687 (Oct.) 1928.

The embryo here reported showed, in addition to the nodule to be described, a reduplication of the central canal in the caudal portions of the spinal cord. Furthermore, there was a small cleft in the roof of the mesencephalon. Microscopic examination of the embryo showed at the level of the fifth lumbar segment a small epithelial nodule projecting into the central canal. This nodule extended over thirteen segments and measured 130 microns. It originated from the dorsal third of the lateral wall of the cord and from the zona ependymates. It was egg-shaped. The epithelial cell proliferation arose from the zona ependymates.

ALPERS, Philadelphia.

TRAUMA DURING BIRTH AS CAUSE OF DIFFUSE DILATATION OF THE ESOPHAGUS. P. H. G. VAN GILSE, Ztschr. f. Hals-, Nasen- u. Ohrenh. **22**:91 (June 16) 1928.

Dilatations of the esophagus are circumscribed, "diverticula" or more or less diffuse. The cause of the latter type is: (1) organic, caused by a stenosis in the

presence of a tumor which leads to a secondary dilatation of the distal end through a formation of a stenosis or diaphragm; or (2) functional, caused by spasm of the muscles at the lower end of the organ at the cardiac or the hiatus diaphragmaticus. Paralysis of the muscle system is also mentioned, especially following diphtheria and in botulism. A lesion of the vagus nerve must be assumed. The animal experiment furnishes similar symptoms. Neuritis of a different etiology (for instance syphilis) and bulbar lesions may also cause paralysis of the muscles. In these instances, pronounced dilatations occur. Idiopathic dilatations may occur without any apparent reason. They appear most often at puberty, but they may occur between the ages of 8 and 10 years.

A female patient of the author had, during her later school years, eaten voluminous meals in great haste. Jackson mentioned as a cause of dilatation also abnormality of the left lobe of the liver, according to Mosher's view, but he localized the spasm at the level of the diaphragm, the "diaphragmatic pinch-cock." Guisez accused poor mastication.

The author mentions, for the first time, a case in which paralysis of the esophagus was caused by a trauma at birth. The patient, a girl, born on May 19, 1926, was brought to Prof. Cornelia de Lange on April 28, 1927. Solid food was vomited. Birth by breech presentation had been difficult. The child did not cry, but whined continuously. On the third day, mucus and blood were still flowing from the nose. The infant took the breast only on the fourth day, but the milk came out of the right nostril. On the fifth day, 50 Gm. of milk was retained. The child opened her eyes only after eight days. In the second week, it was noticed that the left hand and foot were edematous. A month later, the child became still more apathetic and developed pronounced dyspnea while drinking. On June 22, she was extremely sick, had continuous high fever and had to be given epinephrine and camphor. Both arms and legs were flabby. The child was fed with a tube and had improved considerably by June 30. On June 27, solid food was still returned. There was a slight ptosis of the right eye, the pupil was somewhat narrowed and the eyeball was retracted (Horner's symptom). A slight paresis of the left hand and a still slighter one of the left arm prevailed. All muscles of the left hand and the nerves of the left arm and plexus (Erb's point) reacted normally to the faradic current. All muscles of the face on both sides responded promptly to galvanic irritation. There was no reaction of degeneration. Roentgen examination revealed dilatation of the esophagus with paralysis. Lower down spastic symptoms were noted. Esophagoscopic examination in the dorsal position bore out the results of the roentgen examination. After the opening of the esophagus was passed easily, a wide tube was encountered. After a few contractions, a rather firm closure at the hiatus of the diaphragm and at the cardia was noticed. The vocal cords moved normally.

The paralysis was caused by a trauma at birth, probably by one resulting in a hemorrhage in the medulla oblongata at the level of the nucleus of the vagus, most likely in the region of the fibers which innervate the esophagus. In the beginning parts of the central portion which innervate the throat (milk from the nose) and perhaps nuclei innervating the vocal cords (absence of plain sounds) were injured; also contiguous parts of the pyramid tracts were affected. The paralysis of the pharynx was unilateral. This fact was important in this patient, because the first phase of swallowing, the buccopharyngeal, was possible. The paralysis of the esophagus was caused by a bilateral disturbance in the region of the vagus. Unilateral conditions cause only slight disturbances of the esophageal act of swallowing, or none, as Neumayer states. The complex innervation of the lowest portion of the esophagus was recently demonstrated by Jacques and Rousseaux. The vagus is the dilating and the sympathicus the constricting nerve.

The author gives an exact localization of the trauma. During the course of the disease, at the end of June, a relapse of the hemorrhage occurred, perhaps under the influence of an infection. Then the paralytic symptoms were evident. Treatment consisted in regulation of the diet. Frequent meals consisting of finely ground food were given; the quantity and quality were carefully controlled

in regard to calories and vitamins. After about one year of this regimen, the child could eat more solid food, for instance, hard biscuit. If the esophagus was not loaded too much, the fluoroscope showed almost normal conditions. The left arm and hand functioned better. During a severe cold, however, the old disturbance of the esophagus occurred again.

A careful treatment by probes and, finally, Heller's operation might be considered in case the conservative treatment does not lead to any improvement. Besides traumas at birth, the effects of other diseases of childhood must be considered, either through lesions of the nuclei, for instance, in encephalitis, or through effects of toxins, for instance, in diphtheria, which may cause an injury of the innervation of the esophagus. Ylippoe, in his discussion of pathologic anatomic disturbances in premature births, mentioned that hemorrhages in the medulla oblongata can more easily be diagnosed than other hemorrhages in the brain. Besides attacks of asphyxia, two symptoms are rather constant: (1) the impossibility to swallow, and (2) the "jumping-jack" symptoms (on percussion of the sternum).

AMBERG, Detroit.

HEREDITARY SYMMETRICAL HYPOPLASIA OF JOINTS. D. G. ROCHLIN, Ztschr. f. Konstitutionslehre **13**:654, 1928.

Seven instances of symmetrical stiffening of the joints of both hands and feet in four generations of a family with a study of the condition in a father, aged 46, and his daughter are recorded. The anomaly is most commonly observed in the second, third, fourth and fifth interphalangeal joints of the hands and feet. The condition develops without changes in bone absorption and is a hereditary dominant according to the mendelian law.

CONGENITAL DEFECTS OF THE RADIUS AND EAR AND FACIAL PARALYSES. ERIK ESSEN-MÖLLER, Ztschr. f. Konstitutionslehre **14**:52, 1928.

In a girl, aged 6 weeks, the author records the occurrence of asymmetry of the face due to paralysis on the right side associated with furrowed, blunt tipped tongue, apical attachment of the frenulum, bilateral ranula, absence of the muscles of the left ear, absence of the left auditory canal, and deformity of the left upper extremity consisting of kinking of the humerus, ankylosis of the elbow and terminal joint of the third left finger, and complete absence of the radius and the phalanges of the first two fingers. The variations in facial expression due to the paralysis are portrayed. The left upper extremity is carried bent at the elbow with a radial deflection and pronation of the hand. A review of 200 instances in the literature is included. Some of the small bones of the wrist are absent in most instances. Defects of the ear were present in 20; facial paralysis was observed in 100. The latter condition is regarded as a disturbance of the peripheral neuron. The frequency of the occurrence of this condition in the Women's Clinic was 4 among 17,000 new-born infants. The condition may be bilateral. The etiology is somewhat indefinite; internal and external causes such as heredity, phylogenetic radial developmental defects, solitary and multiple genetic irregularities, as well as intra-uterine factors of pressure, faulty embryo enclosures and toxic substances were discussed. The author is inclined to disregard the external factors as causative and holds that, in his case and in most of those in the literature, the etiologic agency is concerned with one or more developmental arrestments in the embryo.

FRANK R. MENNE.

Diseases of the New-Born

STAPHYLOCOCCUS AUREUS CONJUNCTIVITIS OF THE NEW-BORN. ARTHUR B. THOMAS, J. Infect. Dis. **43**:306, 1928.

An acute purulent conjunctivitis may occur in infants without evidence of a preexisting vaginitis in the mother. In 100 consecutive cases of purulent conjunctivitis of new-born infants, none appeared to be caused by the gonococcus.

Cultures of *Staphylococcus aureus*, isolated from the conjunctivitis and some other lesions that were present, seemed to belong to a single strain and were atypical in staining qualities, metabolic reactions with carbohydrates, and in pathogenicity for animals. This organism was considered to be the causative agent in all the cases and was probably transmitted through contaminated olive oil or boric acid or both.

[ARCH. PATH.]

CUTANEOUS INDURATION IN A NEW-BORN INFANT. B. CARDELLE, Bol. Soc. Cubana de pediat. **1**:15 (Jan.) 1929.

An infant, aged 29 days, presented extreme swelling and nodular infiltration of the extremities. There was no history of trauma or syphilis. The lesion cleared spontaneously. Cardelle reviews the literature and discusses the different cases reported. The differential diagnosis is between syphilis and erysipelas. No treatment is necessary. Histologic examinations show an infiltration of giant cells into the dermis.

SANFORD, Chicago.

GANGRENE OF THE FOREARM IN A NEW-BORN INFANT. W. FISCHER, Arch. f. Gynäk. **136**:181 (March) 1929.

A primipara, aged 18, gave birth to an infant weighing 4,000 Gm., after a fourteen hour labor. The right hand had presented at the same time as the head. The mother ran a stormy febrile course and died one week after delivery. The infant developed gangrene of the right forearm, petechiae and edema of the scrotum, ran a septic temperature and died on the eleventh day. At autopsy, thrombi were found in the following vessels: in the full extent of the thoracic aorta, the main branch of the left pulmonary artery, the main branch of the portal vein and in all the large vessels of the right upper extremity. Bacilli were found in the edges of some of the thrombi. Fischer came to the conclusion that thrombi occurred in the vessels of the arm following their injury during labor. The other vascular changes were either embolic or terminal. Normal viscera and umbilical vessels ruled out a primary sepsis. The author stated his belief that the bacteria found in the thrombi were terminal invaders.

BRAHDY, New York.

BIRTH INJURY OF THE BRAIN. W. COHEN, Zentralbl. f. Gynäk. **51**:505, 1927.

During labor at term in a primipara, which was prolonged over several hours, a marked irregularity in fetal heart beats was noted before the head was engaged or the waters had broken. The labor pains were severe. The child was well developed, but had cyanosis and convulsions and died after thirty-four hours. Grossly, there were a number of places in the white substance of the cerebrum which were slightly yellow, and by microscopic examination this color was found to be due to fatty degeneration of the neuroglia. The opinion is expressed that the focal fatty change was caused by the bruising which the head received when jammed against the maternal bony pelvis by the uterine contractions. Hemorrhages were altogether absent.

E. R. LE COUNT.

Acute Infections

WHOOPING COUGH: VACCINE THERAPY OR EARLY DIAGNOSIS. LOUIS W. SAUER and LEONORA HAMBRECHT, J. A. M. A. **91**:1861 (Dec. 15) 1928.

Whooping cough and its complications cause more deaths than do measles, scarlet fever or diphtheria. The injections of a potent vaccine failed to prevent whooping cough in definitely exposed susceptible children, and vaccine therapy had little if any influence on the course in 100 patients. Use of the Chevitz and Meyer cough-plate method is a simple and reliable aid for early diagnosis. With prompt isolation of the patient and exposed susceptible persons, it is, at present, the only reliable means of reducing morbidity and mortality.

BONAR, Salt Lake City.

SUSCEPTIBILITY OF ESKIMOS TO THE COMMON COLD AND A STUDY OF THEIR NATURAL IMMUNITY TO DIPHTHERIA, SCARLET FEVER AND BACTERIAL FILTRATES. PETER HEINBECKER and EDITH I. M. IRVINE-JONES, J. Immunol. **15**:395, 1928.

Eskimos are very susceptible to infections of the upper respiratory tract on contact with the outside world. Ordinary bacterial infections rarely occur. Diphtheria and scarlet fever are unknown clinically. In a group of about fifty subjects all gave negative reactions to the Dick test and also, in the case of the adults, to the Schick test. Children up to the age of 12 years invariably gave positive reactions to the Schick test. Three serums were found to contain antitoxin both for diphtheria and scarlet fever. It is therefore concluded that the immunity to the disease and the negative reaction to the skin tests depend on the presence of antitoxin. This is interpreted as being due to a natural hereditary immunity dependent on some nonspecific antitoxic mechanism. Skin reactions with filtrates of streptococci isolated from cases of rheumatic fever were mildly positive in a small percentage of cases. Neutralizing antitoxin was demonstrated in all three serums but it was not invariably present for all three toxins. The Eskimos showed a high percentage of positive reactions when tested with a *Staphylococcus aureus* filtrate.

[ARCH. PATH.]

THE APPROXIMATION OF THE TOXICITY OF DIPHTHERIA TOXIN IN VITRO. ARTHUR LOCKE and E. R. MAIN, J. Infect. Dis. **43**:420, 1928.

A simple, practicable method is reported, whereby the L_o titer of an unmodified diphtheria toxin may be predicted, in vitro, with an accuracy of from 85 to 95 per cent. The method is based on the use of a formula correlating the properties of toxicity and antitoxin-binding avidity. It consists of a modified flocculation titration, wherein the latter property is evaluated in terms of L_f titer and "unit flocculation time," the results being converted into toxicity units by reference to the basic formula.

[ARCH. PATH.]

THE OPSONIFICATION TEST FOR THE RAPID IDENTIFICATION OF THE STREPTOCOCCUS OF SCARLET FEVER. KATHARINE M. HOWELL and MARIE WERNER, J. Infect. Dis. **43**:525, 1928.

Although the opsonification test for the identification of scarlet fever streptococci is not absolutely specific in our series, it nevertheless offers a rapid, valuable aid in the diagnosis of scarlet fever.

[ARCH. PATH.]

RÉSUMÉ OF THE RESULTS OF THERAPY WITH CONVALESCENT SERUM IN POLIOMYELITIS. J. M. MCEACHERN, BRUCE CLOWN, LENNOX G. BELL and MARY MCKENZIE, Canad. M. A. J. **20**:369 (April) 1929.

Convalescent serum was used extensively in the Manitoba epidemic of 1928.

Serum from six to eight donors who had had poliomyelitis for from a few months to thirty-three years previously was pooled.

Standard doses of 25 cc. of serum were employed in the early stages of the disease. No unfavorable reaction followed its administration.

One hundred and sixty-one cases are reported. Of these, seventy-four patients received the serum in the preparalytic stage; fifty-four received no serum, and thirty-three received the serum too late for it to be of much value; that is, after the onset of the paralysis.

The series is divided into four groups:

Group 1: Fifty-seven patients who received an average of 25 cc. of serum intramuscularly in the preparalytic stage. Ninety-three per cent made a complete recovery. There were no deaths.

Group 2: Seventeen patients who received one or more doses of serum by various routes or more than one dose of serum intramuscularly. The results approximate those of group 1.

Group 3: Thirty-three patients who received serum after the onset of paralysis. Twenty-two per cent made a complete recovery; 33 per cent died, and 45 per cent became paralyzed.

Group 4: Fifty-four patients who received no serum. Twenty-six per cent completely recovered; 63 per cent showed residual paralysis, and 11 per cent died.

The cases were also grouped according to the month in which they occurred and as to whether the patients lived in the city or in the country.

MOORE, Omaha.

SERUM THERAPY IN POLIOMYELITIS. C. LUZ, Arch de pediat., Rio de Janeiro **5**:159 (Feb.) 1929.

Luz gave serum in six cases of poliomyelitis, with good results. He varies the amount with the age of the child, giving from 4 to 16 cc. a day for four consecutive days. The serum must be given early in the disease to have good results. The majority of patients were given serum within twenty hours from the beginning of the clinical symptoms.

SANFORD, Chicago.

TONSILLECTOMY AND SCARLET FEVER. J. ZIKOWSKY, Wien. klin. Wchnschr. **42**:37 (Jan. 10) 1929.

Being convinced that the virus of scarlet fever enters through the pharynx and becomes localized in the tonsils, the author compared the course of the disease in patients who had and in those who had not been subjected to tonsillectomy. Among 1,013 patients, tonsillectomy had been done in 23. In each of the latter group, the "second phase" (zweite Krankheit of Pospischill) was absent. Secondary angina or cervical adenitis did not occur. There was no difference in the incidence of "scarlet heart" or of rheumatism, and a slightly higher incidence of nephritis (7.37 per cent for nontonsillectomized and 8.7 per cent for tonsillectomized patients).

CLAUSEN, Rochester, N. Y.

POSTDIPHTHERITIC STENOSIS OF CICATRICES OF THE LARYNX IN CHILDREN, AND THEIR TREATMENT. MARK PAUNZ, Ztschr. f. Hals-, Nasen- u. Ohrenh. **22**:424 (Jan. 7) 1929.

The postdiphtheritic cicatricial stenosis of the larynx is caused by (1) diphtheria, (2) tracheotomy and (3) intubation. The pseudomembranes in the region of the cricoid cartilage cause grave stenoses not only in the acute stage but also later, whereas the accumulated layers around the glottis scarcely cause later disturbances, but they cause attacks of suffocation in the acute stage. In the region of the cricoid cartilage, the opening is smaller; the submuccosa is richer and more loose, containing many lymph vessels, and it is especially adapted to deep infiltration. When the pseudomembranes are detached, an ulcer remains, which is covered with epithelium. In deep ulcers, vivid granulation occurs which heals slowly. In the region of the cricoid cartilage, a scar results which forms at times a crest, frequently a circular cicatrix and rarely an irregular scar; then again a thick, callous cicatrix with a broad base, which causes a pronounced stenosis and sometimes a total occlusion. While a correct tracheotomy may cause a stenosis, a badly performed tracheotomy, the cricotracheotomy, can more frequently be accused of causing trouble. Intubation can cause decubital ulcers. They can be found where the tube exercises pressure: at the base of the epiglottis, at the arytenoid cartilage and in the region of the cricoid cartilage. The first named ulcers can exist without causing further injury, whereas the ulcers in the region of the cricoid cartilage increase the disturbance. Yet superficial ulcers may heal in spite of intubation. A grave stenosis may even be prevented by intubation. The author reports a case in point. In deep ulcers, the continued use of the tube is injurious, even sometimes if the brass healing tubes of O'Dwyer, (coated with gelatin and Ermold's tubes impregnated with alum powder) are used. In these instances, a secondary tracheotomy is required. J. von Bokay could reduce

the number of cases in which secondary tracheotomy was required to 5 per cent by the use of tubes coated with gelatin and alum, but others have found secondary tracheotomy necessary in 35 per cent or more of their cases. After the tracheotomy, intubation should be continued, according to O'Dwyer and Bokay, but as a systematic method of dilation. It is possible that highly concentrated serums may be the cause of less frequent instances of stenosis.

Paunz now uses Hasslinger's directoscope for diagnostic purposes in children, because it is more perfect and more easily handled than other instruments. Probing is most important. Laryngofissure is the only procedure that allows a good inspection. It is imperative that this method should not be resorted to, however, in cases in which the process of scar formation has not come to a standstill. It is also inadvisable to perform laryngofissure in children under 4 years of age. Treatment consists of (1) creation of a satisfactory opening, and (2) closure of the fistula in the larynx or trachea. In cases of grave stenosis, only extensive excision of the scar tissue and subsequent dilation can lead to success. The author splits the larynx, beginning from the fistula, exactly in the middle line, until the lower or middle third of the thyroid cartilage is reached. Thin, circular cicatricial formation or strings passing over the opening of the larynx are excised. Curvatures are corrected by longitudinal incisions, and a tight tampon coated with an ointment of nitrate of silver solution is inserted. The larynx is closed with two or three catgut sutures. Three or four stitches with fine silk close the skin. A gauze tampon treated with iodoform is fixed at the cannula. It is removed simultaneously with the skin sutures on the sixth day. From then on, the tampons are changed every fourth or fifth day, for from two to three weeks, and their thickness is increased. After three weeks, systematic intubation is used, if possible with larger tubes than the age of the child calls for; with a drainage tube; with a rubber plug, or with a smooth metal plug containing holes for the silk threads that are needed in the introduction of the plugs and in keeping them in place. The rubber tubes or rubber plugs must be changed every third or fourth day, whereas the metal plug can remain in situ for a week or longer.

Sometimes results are obtained in a surprisingly short time. The author reports two such cases. Sometimes the after-treatment takes one or two years. One must be careful not to discontinue treatment too soon. The author used Chiari's or Brueggemann's cannula and, in some instances, a T-cannula. The laryngostoma must be watched carefully. In some cases, Thiersch's transplantations can be used. In addition, circular resection of the larynx may be indicated. Whether Thiersch's transplantations or skin flaps are used, the systematic dilation must not be neglected. After a sufficiently large permanent opening has been obtained, the T-cannula may be removed and the laryngostoma remains open for half a year. Then the fistula may be closed. A two layer suture is used. A larger laryngostoma requires a skin flap. It is advisable to place a periosteum bone flap next to the flap which has the cutaneous surface toward the larynx and next to the second flap. The periosteum bone flap will be resorbed after it has served its purpose. The periosteum bone flap may be taken from the clavicula, sternum, rib, crista ilii or tibia. The author has taken it twice from the tibia, with complete success. He reports a difficult case of this nature and depicts the method. As a last resort, if a sufficient opening cannot be reached by dilatation, or if the resection of the narrowed part of the larynx does not yield a result, a permanent laryngostoma cannot be avoided. Some patients are very much pleased with this result. By lowering the chin to the chest, the patient may produce a loud voice. A boy, aged 11 years, could close the slitlike laryngostoma by simply turning the head to the side.

The author treated nineteen patients with cicatricial stenosis following diphtheria, from 1917 to 1928. Two patients came from other hospitals and eight from the province. In all, sixteen carried cannulas for three months, and for two, three, five, seven and eleven years. Nine patients were treated by laryngofissure with excision of the scar and immediate closure of the larynx. Of these, two were treated by systematic intubation; the other seven with gauze tampons treated with iodoform, and later with rubber drainage tubes or solid rubber and

metal plugs. The time of treatment was from two or three months to one year, in one case two years. In all cases, a complete cure resulted. The fistula in the trachea closed spontaneously in the two patients treated by intubation and in one treated with a rubber drainage tube. In five patients, closure was obtained by the suture in two layers. In a boy, aged 3½ years, the fistula was not treated. It forms a slit 1 mm. wide and 8 mm. long. The boy, now aged 12 years, can breathe freely and speak with a loud voice. In seven cases, the stenoses were grave. Among them were three cases of total occlusion. In three patients (among them two with impermeable cicatricial diaphragm), a complete cure was obtained with subsequent plastic closure of the laryngostoma (twice with implantation of a periosteum bone plate from the tibia, and once with the two layer suture). Two patients are still under treatment. In two cases (in 1921 and 1922), treatment could not be completed for other reasons. The author reports three other cases in which the patients had been admitted without a previous tracheotomy. The author follows up his cases. Of the sixteen patients who carried cannulas, twelve could abandon them entirely. The children developed well. One child died of tuberculous meningitis after the cannula was no longer in use and after the tracheal fistula was closed. The other children did not carry a cannula for from three to nine years. Most of them have a rather good and some even a perfect voice. Twelve illustrations accompany the article.

AMBERG, Detroit.

THE TREATMENT OF EPIDEMIC CEREBROSPINAL MENINGITIS WITH THE SPECIFIC ANTIMENINGOCOCCIC SERUM. H. A. EILER, Pediatriya **12**:309, 1928.

Until 1927, the specific treatment for epidemic cerebrospinal meningitis has not been used at the Children's Hospital of Moscow. The reason for this was the unfavorable report of Dr. Lantz of this hospital, who found in 1914-1916 that the mortality of the disease was not at all influenced by the injection of the antimeningococcic serum. Table 1 shows the mortality rate of children affected with meningococcic meningitis in the years 1925 and 1926, who have not received any serum.

TABLE 1.—*Mortality Rate for Cases of Meningitis in Which Serum Was Not Given*

Year	Number of Cases	Cured		Patients Who Had Sequelae on Leaving Hospital		Patients Whose Condition Was Serious on Leaving Hospital	Died
		Number	Per Cent	Number	Per Cent		
1925	28	6	21.4	8	28.6	2	12
						14 (50%)	
1926	48	11	22.9	14	29.1	7	16
						23 (48%)	

TABLE 2.—*Results in Patients Who Did Not Receive the Serum*

Case	Age	Day of Entrance After the Onset of Symptoms	Day that Improvement Was Noticed	Day that Cure Was Recorded	Day of Return of the Spinal Fluid to Normal	Day that Patient Was Dismissed from the Hospital in Serious Condition	Day of Death
14	2 months	4	23	28	27	..	..
3	6 months	4	0	0	0	26	..
4	6 months	15	0	0	0	36	..
21	1 yr. 8 mo.	28	0	0	0	..	30
22	9 months	15	0	0	0	..	18

During the period between September, 1926, and February, 1927, the author used the antimeningococcic serum in the majority of his patients, using the others as controls. The injection was usually given intraspinally. Tables 2 and 3 show the results obtained.

TABLE 3.—*Record of Injections of Serum*

Number of Patients	Age	Day of Entrance after Onset of Disease	Day of First Injection of Serum	Quantity Injected into Canal, Cc.	Quantity Injected Intramuscularly, Cc.
18	2 years	2	3	40	0
1	2½ years	3	7	60	30
8	1 year, 3 months	3	4	50	10
7	3 years	3	4	85	0
13	7 months	3	4	60	0
19	4 years	4	5	95	0
2	9 months	29	32	30	40
11	5 years	1	3	40	0
15	1 year	3	3	20	0
20	5 years	3	4	30	0
6	2 years	11	11	0	20
9	8 months	18	19	10	10
10	6 months	11	12	20	..
17	10 months	3	4	40	..
5	8 months	8	9	10	10
12	1½ months	7	9	0	20

TABLE 4.—*Results in Patients Receiving Serum*

Serum Sickness	Cured	Died	Dismissed from Hospital in Serious Condition	Duration of Disease, Days
+	+	0	0	14
0	+	0	0	16
+++	+	0	0	47
+	+	0	0	23
+	+	0	0	15
0	+	0	0	48
+++	+	0	0	39
	0	+	0	5
	0	+	0	5
	0	+	0	5
	0	+	0	17
	0	+	0	27
	0	+	0	19
	0	+	0	15
	0	0	+	11
			+	11

The author concludes, therefore, that:

1. Antimeningococcic serum is a good specific means of treating persons with epidemic cerebrospinal meningitis.

2. Antimeningococcic serum has little effect, however, on infants.

3. The best method of injecting the serum is the intraspinal method. The serum should be used as soon as the diagnosis is made. Injections should be given daily and, if necessary, twice a day.

4. It is better to use the monovalent serum. It is necessary, therefore, to secure the help of the laboratory in determining the type of organism.

GASUL, Chicago.

Chronic Infections

TUBERCULOSIS IN CHILDHOOD. BELA SCHICK, M. Clin. N. America **12**:561 (Nov.) 1928.

Behring's postulate that tuberculosis in the adult is only the end of a song sung at the cradle of the infant must be modified to include the whole of childhood. The young infant's natural resistance to tuberculous infection is weak, resulting in a high mortality rate during the first few months of life. During the second half of the first year, however, an increase in resistance develops, which becomes more effective with advancing age.

The classic location of the primary focus of tuberculous disease is subpleural. With the lodgment of the tubercle bacillus in an alveolus or small bronchiolus, there is set up an exudative inflammatory process related to pneumonia. From this point, the infection invades the regional glands, especially those in the bifurcation, by way of the lymphatics. Here the infection is usually arrested for a time, completing the primary stage or primary complex. In favorable cases, the primary focus may entirely heal. The regional glands, however, even in so-called complete cures, may still harbor living tubercle bacilli. Perfect clinical healing requires at least two or three years.

The second stage is characterized by the advance of the infection from the regional glands. There are four routes by which dissemination may take place: lymphatic, hematogenous, bronchogenous and enterogenous. By way of the lymphatics, the infection may travel to the paratracheal glands and finally to the glands in the jugular angle. Subsequently, the tubercle bacillus may pass into the thoracic duct, the superior vena cava, the right side of the heart, and the left side of the heart through the pulmonary circulation, and become dispersed throughout the body. The younger the child and the more active the disease, the greater is the likelihood of massive infection from the site of the primary focus with the development of miliary tuberculosis.

Dissemination by the hematogenous route may result from the direct invasion of the venous part of the lung capillaries by the bacilli, or when erosion of the walls of the pulmonary veins contiguous to caseating glands allows infectious material to find its way directly into the blood stream. In the latter event, as this material is carried directly to the left side of the heart without traversing the entire pulmonary circulation, and without previous filtration in the lung capillaries, all regions except the lungs are exposed to more massive infection.

By the bronchogenous route, infectious material, loosened by the act of coughing, invades other parts of the same lung and frequently the opposite lung. These secondary foci are usually larger than the original focus of infection. The swallowing of infected sputum may result in the enterogenous spread of the disease, with involvement of the intestines and mesenteric glands.

In case widely disseminated infection does not occur, the second stage of tuberculous disease is characterized by attempts at arrest with intermittent manifestations of activity. The disease at this stage is more an exudative than a proliferative process. If infection does not occur until from 7 to 10 years of age, the disease is usually arrested in the first stage. After the organism has harbored tuberculous infection for many years, the reaction of the tissues becomes altered, and proliferation tends to replace exudation. The disease then has a tendency to become localized in the apexes with the formation of chronic cavities. The third stage does not occur characteristically before puberty. SMITH, Ogden, Utah.

HUTCHINSONIAN TEETH: ASSOCIATION AND PATHOGENESIS. C. AUDRY, Ann. de dermat. et syph. **9**:737 (Sept.) 1928.

Audry states that hutchinsonian teeth are a fairly common manifestation of congenital syphilis, more frequent than labyrinthitis, and at least as common as interstitial keratitis.

Hutchinsonian teeth, practically speaking, occur only in cases of congenital syphilis; strictly speaking, they may appear in other disorders. The author says that Hutchinson's triad is exceptionally rare. He has seen it in only three cases. Dental deformities frequently occur with hutchinsonian teeth. A case is described in which the latter was associated with ogival palate and irregular implantation of the teeth.

Notched incisors are the result of faulty development in the superior mandibular buds. The determination of the defect occurs early, and probably before the fifth week of fetal life. Embryologic study is the key to this problem.

[ARCH. DERMAT. & SYPH.]

ABSENCE OF THE XIPHOID CARTILAGE AND ITS VALUE IN THE DIAGNOSIS OF CONGENITAL SYPHILIS. G. J. LANDA, Ann. de dermat. et syph. **9**:985 (Nov.) 1928.

As it had been indicated that the absence of this structure was a stigma of congenital syphilis, the author undertook a serious attempt to determine its significance. He examined 390 children, aged from a few months to 15 years. In nonsyphilitic children absence of the xiphoid was found in 5.5 per cent, while in known congenitally syphilitic children, it was absent in approximately 20 per cent. It is concluded that the absence of the xiphoid cartilage is more frequent in congenital syphilitic children than in nonsyphilitic, but its absence is not pathognomonic of the disease in question.

MICHAEL, Houston, Texas.

EXPERIMENTAL RESEARCHES ON THE NECROTIC LESIONS PROVOKED BY THE INJECTION OF MASSIVE DOSES OF B.C.G. M. J. ZEYLAND and MME. E. PIASECKA-ZEYLAND, Ann. de l'Inst. Pasteur **42**:652, 1928.

Rabbits and guinea-pigs were injected with 15 or 20 mg. of B.C.G. or with killed virulent tubercle bacilli by various routes, intravenous, intra-arterial, intracardiac, intrapleural, intraperitoneal and intrarenal. Rabbits injected intravenously gave noncaseous follicles. Guinea-pigs injected intraperitoneally showed tubercles, sometimes caseous. Part of the rabbits given an intracardiac injection and all given injections in the pleura or in the kidney gave tubercles with necrosis. Necrotic lesions are secured experimentally when conditions permit an agglomeration of bacilli in the tissues. This necrosis is due to endotoxins comparable to those of some of the acid-fast saprophytes. "Under the conditions of vaccination, B.C.G. is inoffensive."

REINFECTION OF TUBERCULOUS GUINEA-PIGS AND GUINEA-PIGS IMMUNIZED WITH B.C.G. M. E. RIST and MLLE. J. MISIEWICZ, Ann. de l'Inst. Pasteur **42**:945, 1928.

Virulent tubercle bacilli were inoculated subcutaneously or into the inguinal glands of a group of guinea-pigs, the survivors being used for reinfection. In another group inoculated with B.C.G. all survived. All reinoculations were intraperitoneal in varying amounts. In general, the results indicate that animals surviving virulent tubercle bacilli on reinoculation die sooner than the control animals — possibly a matter of allergy — whereas animals injected with B.C.G. survived the second inoculation (virulent tubercle bacilli) longer than those in the control group.

TRANSPLACENTAL INFECTION WITH TUBERCULOUS ULTRAVIRUS AND TUBERCULOUS HEREDITY. A. CALMETTE, J. VALTIS and M. LACOMME, Ann. de l'Inst. Pasteur **42**:1149, 1928.

The authors consider the transplacental transmission of the normal form of the tubercle bacillus to be infrequent. It was demonstrated in only three of twenty-six infants of tuberculous mothers. Transplacental transmission of the filtrable ultravirus is much more common. It appears particularly intense after three to six months' gestation in women with developing tuberculosis, especially the pulmonary or meningitic type. Usually these are fatal to the child in the first weeks after birth. Then, since the death rate in the first two months of life of infants born of tuberculous mothers does not appear to exceed 20 per cent, and the number of children of tuberculous mothers born with the ultravirus is greater (perhaps 80 per cent), it may be concluded that perhaps nearly 60 per cent of the new-born carriers of the ultravirus support this infection without immediate harm. There seems to be some immunity. The matter is being studied. Thus far, the distinction between transplacental transmission of the tubercle bacillus and of the ultravirus does not in any way indicate a change from the procedure of separation from the mother or the use of B.C.G.

M. S. MARSHALL.

WASSERMANN-FAST CONGENITAL SYPHILIS IN TWO SISTERS. SCHULMANN and GEORGES-LEVY, Bull. Soc. franç. de dermat. et syph. **35**:836, 1928.

The interest in these cases resides in the fact that two sisters with congenital syphilis were Wassermann-fast, despite every therapeutic endeavor.

[ARCH. DERMAT. & SYPH.]

TUBERCULOUS BRONCHOPNEUMONIA IN AN INFANT. G. GOMEZ DEL RIO, Bol. Soc. Cubana de pediat. **3**:116 (May) 1929.

A child, aged 18 months, presented a typical picture of bronchopneumonia. The temperature was 40 C. (104 F.), the pulse rate, 128 and respirations, 40. The usual treatment was given. A roentgenogram showed that there was considerable consolidation in the upper lobe of the right lung. The condition improved to some extent, but the temperature showed considerable fluctuation. Repeated roentgenograms showed scattered caseous areas. The Mantoux reaction was now decidedly positive. The child died several days later, and an autopsy showed extensive tuberculous bronchopneumonia.

SANFORD, Chicago.

FLARE-UPS OF LATENT SYPHILIS IN CHILDREN. VLADIMIR MIKULOWSKY, Monatschr. f. Kinderh. **43**:21 (March) 1929.

The author describes in great detail two children who, during the course of acute febrile disease, developed obstinate cases of jaundice. As autumn seemed to be the time for the increase in the number of cases of infectious jaundice, this was the first diagnosis made. In making the differential diagnosis the author takes great pains to exclude all diseases mentioned in the textbooks of medicine. As the children showed enlarged livers and spleens, one would think that a diagnosis could be established without such elaborate detail. The diagnosis of syphilis was more confusing in the second case, as the first Wassermann reaction was negative and the child showed marked cerebral symptoms. The suspicion of syphilis was aroused by pigmentation in the retina.

The author calls attention to a few case reports quoted by other observers in which flare-ups of syphilis, such as syphilitic nephritis, were precipitated by intercurrent infections. He repudiates the idea that jaundice itself causes a positive Wassermann reaction and maintains that if a patient has jaundice and a positive Wassermann reaction the jaundice is due to a syphilitic infection.

GERSTLEY, Chicago.

THE BLOOD PICTURE IN TUBERCULOSIS IN CHILDHOOD. L. HINDERSIN, Ztschr. f. Tuberk. **52**:34, 1928.

Hematologic alterations occur on small stimuli. The blood picture, therefore, if critically applied, is of great significance in the therapeutic indication, but its prognostic significance extends only over short periods of time.

MAX PINER.

AN UNUSUAL SKIN ERUPTION IN CONGENITAL SYPHILIS. C. RASCH, Ugesk. f. Laeger **91**:171, 1929.

Two cases are reported of a skin syphilid characterized by a network-like distribution. It is suggested that the infection followed the venous distribution in the skin.

SCHLUTZ, Minneapolis.

TREATMENT OF NEUROSYPHILIS IN THE YOUNG. J. FUKUDA and T. TSUDA, J. Pediat. (Tokyo), Jan. 20, 1929, no. 344, p. 87.

The authors report a case of neurosyphilis first seen in a child at the age of 9 months who was treated by the Swift-Ellis method, without satisfactory results.

The patient was not seen for nearly four years. When the patient suddenly returned to the authors at the age of 4⅓ years, the malarial method was employed with good results. The only changes noted after the institution of the Swift-Ellis method were the lowering of intracranial pressure and the improvement in symptoms in the eye which were the result of increased pressure. After the inoculation of malarial parasites in the same patient at a later stage of the disease, the cerebrospinal fluid became normal in every respect except in the Wassermann reaction. The symptoms which persisted were: subnormal mentality, the positive Wassermann reaction of the blood and cerebrospinal fluid, strabismus, ptosis of the lids, and loss of abdominal and achilles reflexes and knee jerks. No complications of undesirable character were noted during the course of treatment.

KATO, Los Angeles.

Internal Diseases

OPHTHALMIC TEST FOR SENSITIVENESS TO HORSE SERUM. SOPHIE SPICER, J. Immunol. **15**:335, 1928.

The ophthalmic test appears to be safe. Undiluted serum or serum diluted 1:1 or 1:2 can be used. The reactions generally appeared in from ten to fifteen minutes after the application of the serum and cleared up within from one-half hour to two hours. All the patients who gave positive ophthalmic tests gave positive intradermal reactions.

[ARCH. PATH.]

ALLERGY IN CHILDREN. BRET RATNER, M. Clin. North America **12**:847 (Nov.) 1928.

A carefully taken and rationally analyzed history is essential in the study of children with allergic phenomena. This should include not only the history of a typical attack, its relation to foods or contact with animals, its relation to time, seasonal or diurnal, but also the localities in which it occurs, food likes and dislikes, and the antepartum diet of the mother. With respect to the last, Ratner believes that he has demonstrated that children may become sensitized to particular foods of which mothers have eaten excessive amounts during pregnancy. This is brought about by the action of the imperfectly metabolized proteins in the mother's circulatory system on the tissues of the fetus. After birth, the child may develop such allergic phenomena as vomiting, urticaria, eczema or asthma when he partakes of this particular food.

In addition to the history, complete physical examination and laboratory tests, from 300 to 400 skin tests are made on each child by the scratch method. In the case of children showing multiple sensitization, the problem is often difficult and is not to be solved until every substance to which they are sensitive is determined. When a child is sensitive to house dust, the particular substance in the dust to which he is sensitive must be sought. In those who react to but one substance, the problem is much more simple and the avoidance of a particular food or of contact with such material as rabbit hair often brings about brilliant cures.

The author urges that each case of sensitization, however slight, be carefully studied and that such studies be broadly viewed as an important contribution to preventive medicine.

SMITH, Ogden, Utah.

THE TREATMENT OF HEADACHE IN CHILDREN. R. C. LIGHTWOOD, Lancet **1**:770 (April 14) 1928.

Headaches in the young, especially in infants, are comparatively uncommon. Cephalic pain, which may be taken to include headache and earache, causes young infants to put their hands to their heads, scratching them and rubbing them at times; it also causes wrinkling of the forehead, crying and restlessness. Earache is by far the commonest cause of screaming and of putting the hands up to the head; it is especially frequent in association with teething and catarrhs of the

first two years. Apart from earache, true headache may occur in infants and is often a sign of an organic disease of the brain, such as meningitis, intracranial tumor or hydrocephalus. The persistent crying of syphilitic infants has been ascribed to headache resulting from meningo-encephalitis. Eye strain is the commonest single cause of headaches which are prolonged over more than a few days. It seldom occurs before the age of 5 years. The headache of ametropia is commonest after school hours, thus contrasting with toxic headaches which occur mostly in the morning.

A large number of conditions may be responsible for toxic headaches. All the acute infections may produce them, but less commonly than in adults. Fever of less than 104 F. rarely causes this symptom and if it should do so, suspicion of tuberculous meningitis should be aroused. Ordinary toxic headaches associated with an acute infection may be safely relieved by acetylsalicylic acid in doses of 5 grains (0.324 Gm.) every four hours in a child of from 5 to 10 years of age. A morning headache occurs in some children who have a prolonged disturbance of digestion. Such children are most commonly below the age of 7 years and are found to have furred tongues, foul breath and impaired appetite; constipation and abdominal distention may also be present. The digestive disturbance may be dietetic; in this case, proper food should be selected and nothing should be eaten for two hours before bedtime. Stomachic mixtures are useful but subsidiary. Digestive disturbances may also be due to infections of the upper respiratory tract. They are common with chronically infected tonsils and adenoids, which result in the swallowing of secretions.

Headaches due to juvenile rheumatism occur in children of the hospital class above the age of 6 years, and usually in the early part of the day. For the headache of chorea, 5 or 10 grains (0.324 or 0.69 Gm.) of acetylsalicylic acid, according to age, is useful. Migraine, while uncommon, is seen occasionally during the latter half of this period. It has a tendency to be accompanied by pyrexia. There is considerable evidence in support of the view that migraine is manifested in the child by cyclic vomiting. For recurrent bilious attacks accompanied by headache and due to acetonuria, dextrose is an efficient remedy. For young children, a teaspoonful of commercial dextrose three times a day should be used. Persistent headache is found in a certain small group of children with obesity; it is also a feature of dystrophia adiposogenitalis and is often complained of by girls at the age when menstruation commences. Endocrine therapy, analgesics and bromides may all be used in treatment. Headache occurs in about 50 per cent of all cases requiring operation for adenoids. Septic tonsils, dental caries, uremia, nephritis, anemia, trauma, lead poisoning, juvenile paresis and hysteria may all produce this symptom. Sinusitis is an exceptional cause in childhood and only occurs at the end of this period. The cause frequently is not discoverable. Occasionally a family history can be obtained.

PETERSEN, Montreal.

THE CEPHALIC METASTASES OF SUPRARENAL BLASTOMATA IN CHILDREN. DAVID M. GREIG, Edinburgh M. J. **36**:25 (Feb.) 1929.

Greig appropriately calls attention to the primary origin in the suprarenal glands of the tumor which is often found in the orbit; he describes also the bony changes that are found in the cephalic metastases, features which have received little attention in the literature. The metastasis in the head occurs by way of the soft tissues and does not arise within the bone itself. These tumors are neuroblastomas rather than round-cell sarcomas, and they spread through the lymph and not through the blood vessels. The tendency to cephalic metastasis was regarded as a syndrome by R. Hutchison in 1908.

Greig reports a case in a boy, aged 11 months, in whom the first clinical evidence was a disease of the right eye with proptosis, and a right temporofrontal swelling, soon followed by displacement of the eyeball forward, downward and medially. A roentgenogram showed an unusual shadow and some destruction of the lateral bony wall of the orbit. Rapid growth of the tumor, increase in the

breadth of the face with swelling in the region of the left zygomatic arch, a change in the smooth character of the tumor to a nodular type with bony projections, and a relaxed skin were features in the rapid course. Anemia, irregular fever, photophobia, inability to close the eyelids, corneal ulcer, collapse of the eyeball, restlessness or drowsiness, screaming and, finally, jaundice of the skin and ecchymosis of the right eyelid were manifestations during the 110 days that the patient remained in the hospital before death.

The autopsy was complete, and included gross and minute examination of the macerated skull. The only observation of importance outside of the head was the large, soft, purple hemorrhagic-appearing tumor which had destroyed and replaced the right suprarenal gland, the pressure from the tumor having been the cause of the jaundice. The cephalic metastases were numerous. Greig discusses the observation of Frew that a right neuroblastoma usually, but not always, results in a right-sided cephalic metastasis. Involvement of the left side may produce left cephalic metastasis. Bilateral proptosis has been reported from left primary suprarenal growth.

In Greig's case, metastases were principally found in the contiguous portion of the right frontal, parietal, sphenoid and zygomatic bones, but the process is not a real osseous metastasis. The bone is invaded from without. Other changes in the head involved the occipital, maxillary and mandibular bones. The gross manifestations were osteoporosis with outgrowth of bony spicules.

From the fact that neuroblastoma is the most common suprarenal tumor in children and that it does not undergo cephalic metastasis in adults, one concludes that there is increased viability of the cells in such tumors in children, and there is more encouragement to the growth of tumor cells in the tissues of young, vascular, growing persons. The activity of the bone cells is due to the excess of vascularity produced by this highly vascular tumor. NEFF, Kansas City.

SWIFT-FEER ACRODYNIA: ITS RELATIONSHIP TO EPIDEMIC NEURAXITIS. L. VAN BOGART, J. de neurol. et de psychiat. **28**:118 (Feb.) 1928.

A case of acrodynia is described in an adult who developed a neurodermatologic syndrome characterized by an extreme asthenia, considerable pain of the skin and muscles, an intense prurigo, trophic ulcers and generalized muscular hypotonia. To this visceral symptoms were added: spasmodic constipation, gastric symptoms, arrhythmic tachycardia and hypotension. A lumbar puncture disclosed hyperalbuminosis and hypoglycorrhachia. The author is inclined to consider acrodynia as a syndrome of infectious origin involving electively the sympathetic system. He is unwilling to accept the identity with epidemic encephalitis which such investigators as Janet, Pierre and T. Knifer have established. The absence of myoclonia and of ocular disturbances and the dissociation between hyperglycemia and hypoglycorrhachia in the majority of cases contribute to this differentiation.

FAMILIAL PLEONOSTEOSIS. COHEN and DE HERDT, J. de neurol. et de psychiat. **28**:395 (June) 1928.

Under the name of pleonosteosis, André Léri described, in 1921, a variety of dystrophy of the bone which followed an hereditary and familial course; it was characterized by hypertrophy, especially of the epiphysis, and, because of considerable bony development, led to ankylosis or at least to a limitation in movements. The authors describe two cases occurring in the same family. These show, besides the changes in the bone, other anomalies of the cervical region, lack of development of hair, a varus foot and some mental debility. The brother of the patient presents a small palpebral fissure, a prominent zygomatic apophysis, mongoloid features, cryptorchidism and a washed-out expression of the face. Pleonosteosis differs from achondroplasia which is not familial and involves the bones from the intra-uterine stage of life, its evolution ending with birth. Achondroplasia involves only the radicular segments of the extremities.

FERRARO, New York.

MESENTERIC LYMPHOSARCOMA. BOLIVAR DELGADO CORREA and A. VOLPE, Arch. latino-am. de pediat. **23**:89 (Feb.) 1929.

Abdominal localization of lymphosarcoma is rare. The authors report a case in a girl, aged 4 years.

The disorder began with symptoms resembling acute peritonitis. A tumor mass developed rapidly and within a month completely filled the abdomen. There was much paroxysmal pain, and severe cachexia developed before death.

The tumor mass was confined to the mesentery, was highly vascular and entirely made up of lymphoblastic sarcomatous tissue.

SCHLUTZ, Minneapolis.

CYANOSIS OF POLYCYTHEMIA IN A CHILD, AGED SIX YEARS. F. HURTADO, Bol. Soc. Cubana de pediat. **1**:3 (Jan.) 1929.

Hurtado reports the case of a boy, aged 6 years, who became cyanotic during the injection of a vaccine. Examination of the blood showed 70 per cent hemoglobin, 6,300,000 red cells and 9,500 leukocytes. As this increase of red cells is not so marked as in many cases of polycythemia, the author states his belief that there must be some other contributing factor. In this case, the adenoids were markedly enlarged. The treatment in these cases, therefore, is to remove, either medically or surgically, any such contributing factors.

A CASE OF SACROCOCCYGEAL TUMOR. G. TERJERÁ, Bol. Soc. Cubana de pediat. **1**:26 (Jan.) 1929.

A child, aged 9 years, presented no particular symptoms except occasional enuresis and colitis. The result of the physical examination was negative; the blood showed hemoglobin 75 per cent, red cells 4,530,000 and leukocytes 14,500. A roentgenogram showed a sacrococcygeal tumor. Terjera discusses the posssibility of the tumor being a complication of spinal bifida, or a teratoma. The surgical treatment is also in doubt, owing to the possible destruction of vital tissues in removal, and the possible degeneration of a malignant tumor.

SANFORD, Chicago.

INFANTILE KALA-AZAR. MARIANO BENAVENTE, Pediatría españ. **17**:293 (Aug.) 1928.

The author found that the hen was apparently a susceptible host of the virus *Leishmania*. He was able to recover, from the liver of the animal, forms which resembled early types of the flagellate Leishman organism.

This observation is interesting, since it is generally believed that kala-azar is a disease transmitted largely by hematophage insects such as those which transmit malaria and that man is the principal host although numerous authors have shown that the dog is also quite a common host.

The bed bug is regarded by numerous observers as a carrier of the disease. The author states his belief that the domestic fowl is a carrier.

He also expresses the opinion that the organism does not enter by the blood stream alone, but can enter the human host through the gastro-intestinal canal.

SCHLUTZ, Minneapolis.

PERNICIOUS ANEMIA IN CHILDREN. M. FRANK, Arch. f. Kinderh. **86**:13 (Dec. 28) 1928.

A girl, aged 2 years, was seen at the clinic with the characteristic lemon yellow pallor of pernicious anemia. The blood serum was dark golden and contained considerable urobilinogen. The blood showed 1,375,000 red cells, color index 1.7, 4,340 white cells, and 90,000 platelets. There were also normoblasts, anisocytes, poikilocytes and megalocytes. One day later, the child developed an infection and had a high temperature for two weeks. One month later, she returned to the clinic with no sign of the lemon yellow color. There was no urobilinogen

in the serum, and the blood picture had changed. The red blood cells were 4,240,000, leukocytes 6,600 and the color index 0.68. There were no abnormal cells.

The past history was unimportant except that about a year before presentation the child had been in the country and had been given one-fourth liter of goat's milk a day. Frank doubts whether this could have caused the characteristic picture of pernicious anemia, or whether the condition could have been caused by intestinal parasites. He presents the case for study.

SANFORD, Chicago.

TWO RARE OBSERVATIONS IN OXYURIS INFESTATION OF MAN. HELMUTH NATHAN, Frankfurt. Ztschr. f. Path. **36**:82, 1928.

In a case of perirectal abscess, oxyuris was found surrounded by a granulation tissue in which there were many foreign body giant cells. In another case of cirrhosis, ova and embryos of oxyuris were found in cystlike structures in the spleen. The location of these was explained by a retrograde passage from the portal blood stream, this being favored by the portal stasis which the cirrhosis had caused.

JEAN OLIVER.

A CARCINOMA IN A THREE YEAR OLD CHILD. P. ROSTOCK, Virchows Arch. f. path. Anat. **267**:352, 1928.

A tumor of the sacrum, removed from a child, aged 3, proved to be an adenocarcinoma. This was not a carcinoma of the rectum in the ordinary sense, but may have originated from remains of the embryonic caudal gut.

B. R. LOVETT.

THE ABSORPTION OF INSULIN FROM THE MUCOUS MEMBRANES OF THE MOUTH. OTTO OLSEN, Ugesk. f. Laeger **91**:173, 1929.

A lozenge containing insulin, or from ten to twenty drops of insulin, may be placed under the tongue and the dosage repeated several times a day. Considerable insulin is absorbed in this manner in from one to two minutes. This form of treatment is suggested for patients with a mild form of diabetes, for those who are careless about asepsis and for those who refuse injections.

SCHLUTZ, Minneapolis.

HEMATOPORPHYRIA CONGENITA. K. MATSUOKA, Japan J. Dermat. & Urol. **28**:1 (June) 1928.

The author gives a report on three new cases of hematoporphyria congenita, making a total of nineteen in the literature. In his cases early in life there appeared on the face and on the dorsum of the hands and feet a vesicular eruption with serous content. The eruption healed with drying up of the crusts and was followed by atrophy, superficial scarring and hyperpigmentation. The spleen was palpable in two cases in which the urine was the color of port wine. The red cell content and the hemoglobin content were 20 per cent below normal in these two cases. The third case showed only the skin eruption. When the patients were kept indoors and protected from the sunlight, the eruption disappeared.

The author concludes that these patients are sensitive to something in the sun's rays which causes a gradual hemolysis which in turn results in an enlargement of the spleen. Extensive spectral investigations were carried out with the urine containing porphyrin.

MCCARTHY, Washington, D. C.

TYPES OF PNEUMOCOCCUS IN EMPYEMA OF CHILDHOOD. Y. SAKAMOTO, J. Pediat. (Tokyo), Jan. 20, 1929, no. 344, p. 153.

The author examined the types of pneumococcus in thirty-eight cases of empyema and twenty-two cases of pneumonia in patients entering the Tokyo

Imperial University Hospital. The types were determined by the agglutination method only, the stock culture sent by the Rockefeller Institute being used. The pneumococcus was recovered in 80 per cent of all cases; of this group 65 per cent were type IV, and 20 per cent type II. In one patient, both type I and type IV were demonstrated at two different examinations. The streptococcus and the staphylococcus were seen in 5 per cent of the cases. As to the prognostic significance of these types, the author states that in the patients showing Type II the mortality was the greatest (44 per cent), and the next greatest was found in those showing type IV (23 per cent). The mixed infection was found to yield the greatest mortality.

KATO, Los Angeles.

Nervous Diseases

NEISSERIA SUBFLAVA (BERGEY) MENINGITIS IN AN INFANT. HARRIET BENSON, ROSE BRENNWASSER and DOROTHY D'ANDREA, J. Infect. Dis. **43**:516, 1928.

This report describes the clinical progress, the bacteriology and the results of the postmortem examination, including an extended account and the results of the alterations in the brain, of a chronic meningitis in a child 7 months of age from whose spinal fluid *N. subflava* was repeatedly isolated. Anatomically, there was a marked internal hydrocephalus and a pressure displacement by a circumscribed abscess of the tissues of the inferior portion of the cerebellum and the upper part of the spinal cord.

The prolonged mild course of the illness continuing for about three months was a notable clinical feature. Gram-negative diplococci observed in stained preparations of spinal fluid commonly are considered to be meningococci. This conclusion cannot be safely made without careful study of the organisms in culture mediums and by serologic tests. Although the members of the flava group as well as *N. catarrhalis* and *N. sicca* have little pathogenicity in human hosts, they seem to be able to produce disease in susceptible persons.

[ARCH. PATH.]

ENCEPHALITIS RESPIRATORY SEQUELAE. H. G. WOLFF and W. G. LENNOX, J. Nerv. & Ment. Dis. **68**:337 (Oct.) 1928.

Respiratory abnormalities following encephalitis, as reported in the literature, may be grouped as follows: (1) disorders of the respiratory rate; (2) dysrhythmias, including breath holding, sighs and forced expirations, and (3) respiratory ticks, such as yawning, hiccoughing, spasmodic coughing and sniffling.

Three cases are studied by the authors, with two varieties of generalized convulsive reaction besides the respiratory phenomena. In one case, the convulsion began independently of the respiratory attack. In the other there was a simple loss of consciousness with convulsive movements appearing after prolonged apnea, in which the respiratory and accessory muscles were in spasm.

Forbes, by increasing the intrathoracic pressure in cats by rapid inflation of the lungs, showed a definite evidence of stasis in cerebral circulation with subsequent convulsive movements of the animal. When the intrathoracic pressure was allowed to return to normal, the cerebral circulation reestablished itself and the convulsions ceased. This helps one to understand the loss of consciousness and convulsions in these postencephalitic respiratory disturbances.

In normal persons, prolonged overventilation of the lungs will produce tetany, as shown by Collip, Bachus, Grant, Goldman and others. Blood drawn during the period of hyperpnea showed a decrease in plasma bicarbonate and chloride, similar to that obtained during periods of overventilation in two healthy subjects. Ingestion of from 9 to 16 Gm. of ammonium chloride reduced the plasma bicarbonate from 56 to 43 per cent by volume and it was observed that the attacks were temporarily reduced. Under an increase of plasma bicarbonate to 63 per cent by volume there was an increase in the number of attacks. Thus, the patient was better under acidosis and worse with alkalosis.

The author does not attempt to throw any light on the pathogenesis of the respiratory attacks, but believes that there is a definite relationship between the intensity of the respiratory seizures and the chemical composition of the blood.

INVERTED POSITION IN CHILDREN'S DRAWINGS: REPORT OF TWO CASES. GERALD H. J. PEARSON, J. Nerv. & Ment. Dis. **68**:449 (Nov.) 1928.

As Putnam has shown, an object perceived is projected on the retina as an inverted image, and this remains inverted in the visual cortex, for the upper and lower halves of the retina are repeated in the upper and lower lips of the calcarine fissure. The reinversion of the image, so that the object is seen right side up, is a learning process, which probably occurs very early in life when the child is unable to indicate his difficulties to other people. Traces of this period of learning can be found in drawings of children of the preschool stage.

In two patients, one a girl, aged 6, with an intelligence quotient of 60, and the other a boy, aged 5 years and 5 months, with an intelligence quotient of 97, the majority of objects were drawn upside down. When the object was placed upside down, the first child drew it right side up. In both children the motor coordination was poor.

Stern has shown that only very young children can recognize pictures as easily when upside down as when right side up. Spiller reported the case of a boy, aged 8, who saw everything upside down after an attack of measles. In adults, cases of a temporary disturbance of this sort have been reported by authors after head injury.

HART, Greenwich, Conn.

SHYNESS. F. A. HAMPTON, J. Neurol. & Psychopath. **8**:131 (Oct.) 1927.

Shyness is so common that often it is accepted as something inborn, as a characteristic part of the charm of youth, of a certain fineness of character. As the cause of a great deal of mental discomfort, however, shyness is deserving of more attention. McDougall has suggested that schizophrenia is essentially an exaggerated degree of what, in normal people, one calls embarrassment. In certain cases of shyness one sees a habitual smile, in others a mask-like expression. The resemblance to schizophrenia, however, does not extend to the emotions; shy people are capable of great depth of feeling.

It is suggested that the shy person in general suffers from a conflict between the urge to reach upward to the normal level from a position of imagined inferiority and the deterrent fear of failure. The feeling of inferiority, to which this conflict in shyness is attributed, is of the kind which Adler has described and emphasized. It is never one that the shy person admits to himself. An inferiority that cannot be concealed, such as an obvious deformity, seldom causes shyness. The feeling of inferiority may have originated as a sense of cowardice, an inability to play games, a real or fancied absence of physical attractiveness, or as a result of comparison of self with a superior older brother. Most of the reactions of shyness are due to fear of being looked down on, a result especially dreaded by the shy person since it would confirm the suspicion of inferiority which he dimly feels but hopes is unfounded. A meticulous attention to behavior results in extreme selfconsciousness which, however, is not the same as shyness. A well dressed woman may be exquisitely selfconscious and not shy. Much of the painful feeling of shyness may be due to the inhibitions of the conative side of fear. Blushing is an occasional accompaniment of shyness, but is a typical manifestation of anger. It represents resentment against the person who causes embarrassment. There appears to be some relation between shyness and the commonest form of stammer. The former might be compared with a conversion hysteria and the latter with an anxiety neurosis. An advantage of shyness is suggested by La Rochefoucauld's observation that a sure way to predispose any one in our favor is to appear at a disadvantage before him.

As to treatment, the magic formula which will impart selfconfidence is yet to be discovered. Suggestion may help. But the surer and more satisfactory

method of treatment is to help the patient trace the source of his feeling of inferiority; when this is fully disclosed, he is seldom unable to deal with it effectively.

FAVILL, Chicago.

THE ETIOLOGY OF MONGOLISM. HUBERT ARMSTRONG. Brit. M. J. **1**:1106 (June 30) 1928.

Is mongolism inherent in the unfertilized ovum or is it acquired after fertilization? The idea that mongolism is imparted to the ovum in fertilization is not so tenable since evidence appears to point to the maternal factor so constantly. An argument in favor of postfertilization of the embryo is that mongols are often the subjects of other congenital abnormalities. It is argued that the mongolian characteristics originate during the first six weeks of intra-uterine life. On the other hand, an ovum which already contains an inherent defect is more likely to develop other abnormalities than one which does not. David Grieg said that mongolism "seems rather to be a defect in growth (foetal) than a defect in development (embryonic)." He stated that "even from the skull alone there seems evidence that development normally begun has mapped out all the structures and features in the embryo, but has failed to lead them to perfection during foetal growth . . . this failure in the bones is accompanied or followed by defective growth elsewhere, notably in the nervous system."

Armstrong believes that whatever the almost undeniable maternal influence may be, it is exercised on the ovum during its maturation, and therefore before fertilization has followed and segmentation started. The chief argument in favor of this theory is the occasional occurrence of twins, one of whom is a mongol and the other not. There have been about three known instances of twins who were both mongols. The original records of these cases, however, are so inaccessible that although the twins were of the same sex, complete proof that they resulted from uniovular pregnancies is wanting. The fact, however, can be assumed. There are also three cases on record in which the twins were of the same sex, one being a mongol; proof of uniovular pregnancy is lacking here also. The records, however, do not show an instance of mongolism in twins of different sex.

PETERSEN, Montreal.

ENCEPHALO-MYELITIS IN VIRUS DISEASES AND EXANTHEMATA. H. M. TURNBULL, Brit. M. J. **2**:331, 1928.

Focal histologic changes extend from the cortex of the brain to the lumbosacral cord in postvaccinal encephalitis. Acute changes noted in persons dying from fourteen to seventeen days after vaccination consist of slight intermittent infiltrations of the leptomeninges, chiefly about the veins, with small and large lymphocytes, plasmacytoid and true plasma cells, large mononuclear leukocytes and endothelial cells. The essential change consists of perivascular and marginal zones of demyelinization which form wide sleeves, especially about the veins, and extend along their branches. In the subacute type, the adventitial sheaths are distended with a mosaic of large fat granule cells. Turnbull suggests calling the condition disseminated encephalomyelitis of the postvaccinal type, since it differs from poliomyelitis and epidemic encephalitis and belongs in a group characterized by demyelinization as the disseminated myelitis of Westphal and disseminated sclerosis.

ENCEPHALO-MYELITIS IN VIRUS INFECTIONS. J. MCINTOSH, Brit. M. J. **2**:334, 1928.

Two theories are advanced to explain the occurrence of postvaccinal encephalitis: first, that the disease is vaccinal in origin, and second, that it is due to the presence of dormant virus stimulated into activity by vaccination, which virus may be that of poliomyelitis epidemic encephalitis, herpes febrilis or some unknown virus. The arguments McIntosh uses to support the first theory are as follows:

Intracerebral inoculations of neurotropic strains of variolous lymph produce an encephalitis in rabbits presenting the main histologic characters of postvaccinal encephalitis. Intravenous injections of neurotropic strains of vaccinia produce focal lesions in the internal organs similar to those found at times in cases of postvaccinal encephalitis and in variola. He reports the failure to produce any of the known virus infections of the central nervous system by animal inoculation with material from postvaccinal encephalitis. The occurrence of a similar cerebral lesion is reported in a case of encephalitis following smallpox.

GEORGE RUKSTINAT.

ACUTE CEREBELLAR ATAXIA. W. A. ALEXANDER, Edinburgh M. J. **36**:37 (March) 1929.

A boy, aged 3½ years, entered the hospital four weeks after an attack of measles and seven days after the appearance of a left frontal headache. He began to vomit and lost control of balance and movements. The headache and vomiting soon stopped, but the patient then developed extreme ataxia and inability to sit up. Nystagmus was present. Soon improvement began, and after three months no ataxia remained. The only sequel was a tendency to fatigue and excitability. Acute cerebellar ataxia has been found occasionally as a sequel of acute infectious diseases, and its prognosis is good. Encephalitis can be a complication of the exanthemas, and in this case was cerebellar.

NEFF, Kansas City.

TREATMENT FOR EPILEPTIC MANIFESTATIONS BY PHENYLETHYL MANONYLUREA. JACQUES LEYRITZ, Encéphale **23**:787 (Nov.) 1928.

This work is based on twenty-one patients with essential epilepsy who had been under observation since 1922, and had been started on phenobarbital in May, 1926. The total number of attacks suffered by the twenty-one in these years was as follows: 1922, 1,091; 1923, 1,174; 1924, 1,211; 1925, 1,212; 1926, 706, and 1927, 161. This drop in response to the new medication is certainly graphic. The effective doses ranged from 0.1 to 0.04 Gm. In addition to definite action on the epileptic attacks, it exerted a most beneficial influence on the psychic equivalents —several cases being cited in support of this. Some evidence is also adduced that mental deterioration is less noticeable under its use.

AN UNUSUAL FORM OF HEREDITARY FAMILIAL DISEASE. M. SEREJSKI, Encéphale **23**:821 (Nov.) 1928.

The cases of four siblings, three men and a girl, aged 28, 22, 20 and 19 years, respectively, are reported with a symptom complex as follows: auditory disturbances without involvement of the vestibular portion of the ear or nerve, speech difficulties, retinitis pigmentosa, hemeralopia, dermographism, acrocyanosis and some degree of involvement of mentality. Tendon reflexes were exaggerated; there was evidence of hyperpituitarism —marked development of the lower jaw, hypertrichosis, increased metabolism and absence of sexual desire. The onset was insidious and occurred during childhood. Three other members of the same family were normal, as were the parents; five children died in infancy of infectious diseases. Syphilis could fairly be excluded. The author considers the condition a form of familial disease not definitely classifiable with any existing type, although related to amaurotic family idiocy.

ANDERSON, Kansas City, Mo.

A CASE OF POSTENCEPHALITIC TREMOR. A. ABALLI, Bol. Soc. Cubana de Pediat. **1**:36 (Jan.) 1929.

A boy, aged 3 years, gave a history of repeated convulsions, with an accompanying acidosis and intoxication. On presentation, he showed involuntary movements and tremors. The reflexes were absent, and the electrical irritability was 5 ma. All laboratory tests gave negative results. The author states his belief that the tremor was postencephalitic.

CEREBRAL TUMORS OF INFANCY. A. ABALLI, Bol. Soc. Cubana de pediat. **3**:155 (March) 1929.

Aballi states his belief that Cushing's classification of tumors is the most satisfactory. The symptoms will, of course, depend on the location of the neoplasm, but in their probable order of importance they are: dizziness and lack of concentration, vomiting and convulsions.

Circulatory and gastro-intestinal symptoms in turn depend on the parts involved. The author considers these as almost a tumor syndrome. Spinal puncture is of value if hypertension and albumin are shown.

SANFORD, Chicago.

INFANTILE CEREBRAL PALSIES. LUCIANO MAGNI, Riv. di patol. nerv. **33**:231 (March-April) 1928.

This paper is a fairly complete and thorough review covering the interesting and difficult field of infantile cerebral palsies, or — using the more adequate term of Brissaud — infantile encephalopathies. Discussing at first various tendencies, the author points out the fallacies of a one-sided approach to this complex subject. He reviews briefly the etiologic factors of infantile encephalopathies: abiotrophies, syphilis, hereditary predisposition, etc. With regard to syphilis the author judiciously keeps himself to the golden middle course where most probably the truth is found. He then discusses the pathologic changes of infantile encephalopathies: tuberous sclerosis, Strümpell's diffuse sclerosis and cerebral lesions with a tendency to affect the basal ganglions—Wilson's hepatolenticular degeneration, and Vogt's status marmoratus and status dysmyelinizatus.

The most interesting part of the review is that in which clinical forms and neurologic syndromes of infantile encephalopathies are reviewed. Instead of the usual narrow classification into two syndromes, infantile hemiplegia and cerebral diplegia, Magni describes in a masterly way the syndromes of double athetosis, pyramidostriatal disease, infantile pseudobulbar palsy, mesencephalostriatal disease of decerebrate rigidity, chorea congenita, etc. A brief but complete synthetic review of the pathophysiologic data obtained in later years concerning extrapyramidal disturbances makes this clinical part of the paper most helpful in obtaining an orderly orientation in this field of neuropediatry.

Any worker in such institutions as schools for the feebleminded, hospitals for epileptic patients and neurologic departments of children's hospitals will find an important synthesis in this paper.

YAKOLEV, Palmer, Mass.

THE EFFECT OF OUTDOOR SCHOOLS AND SUNBATHING ON THE CHVOSTEK SIGN IN INFANTS. H. BISCHOFF, Arch. f. Kinderh. **86**:20 (Dec. 28) 1928.

Because of the effect of sunbathing on the vegetative and peripheral nervous system, Bischoff reviewed the literature to ascertain its effect on Chvostek's sign of facial irritability. He found that sunbathing, together with outdoor life in general, had a favorable effect on the irritability, but that the results were not uniform.

SANFORD, Chicago.

CONSTITUTION, PREDISPOSITION AND HEREDITY IN EPIDEMIC ENCEPHALITIS WITH SPECIAL CONSIDERATION OF CONSTITUTIONAL AND RACIAL FACTORS. ERNST PEUST, J. f. Psychol. u. Neurol. **37**:233, 1928.

The clinical material at the basis of this contribution consisted of 124 patients with epidemic encephalitis treated between 1921 and 1926 at the University Nerve Clinic in Halle. There were 68 males (among these 7 boys) and 56 females (among these 5 girls). Most of the patients belonged to the lower social strata. The occupation of most of them necessitated prolonged exposure to dust and dirt. Seventeen patients had had some nervous or mental disease prior to the onset of the encephalitis.

From the point of view of constitution, the entire material is divided into four groups: 1. Patients who, in addition to having various partial disease anlages such as cranial bone anomalies, narrow flat chests, kyphoscoliosis, general muscular debility and atony, are also of a generally feeble constitution. These factors, however, seem to be only of secondary importance as far as the development of encephalitis is concerned. 2. A type of constitution which seems to favor the development of encephalitis to a greater degree than in the first group. These persons, in addition to having a marked predisposition to rickets and scrofula as well as to an anlage to the exudative diathesis, also show evidences of disturbances in physical and mental development — perhaps on an endocrine basis. 3. A group which seems to favor the development of encephalitis to a still greater extent and includes persons of the lymphatic constitution with a marked tendency to tonsillitis, angina lacunaris, grip and hypertrophied tonsils, occasionally associated with herpes labialis. 4. Patients with physical or mental infantilism and retarded sex maturity, who seem to be most predisposed to encephalitis. In addition to these four groups the material also contains a large number of persons who show no particular constitution or type that would favor the development of encephalitis. The number of females with pathologic constitutional characters exceeds that of males by almost one-third. This is probably because so many of the former show retarded sex maturity and half of these show, in addition, psychic infantilism. The author's statistics would seem to show that retarded sex maturity, associated with infantilism on a possibly endocrinous basis, may be of significance in the pathogenesis of epidemic encephalitis.

In two cases, the encephalitis appeared at the end of the puerperium; in a third case the mother of an infant born with encephalitis gave a history of severe grip during pregnancy; the succeeding two pregnancies of this mother resulted in abortions. Another interesting case was that of a woman, aged 43, who developed encephalitis during the puerperium; at this writing the child is living but is puny and feeble; although the encephalitis in this case is progressive with increasing inhibition of motility, the mother had given birth to another child three years after the onset of the disease; this infant, however, lived only four months; it was puny and had a tendency to inguinal and scrotal hernia. Two years after the death of this child, she gave birth to a child who was well developed and is still living. The encephalitis in this case is parkinsonian in type. Prior to the illness, this woman had given birth to six normal children. Another patient developed encephalitis early in February, 1922, and had a stillbirth at seven months; the encephalitis was preceded by a stay in bed on account of rheumatism which was followed by a period during which she was somewhat confused, had headaches and high fever; this condition merged gradually into a typical epidemic encephalitis with lethargy and increasing motor inhibition. The child with the congenital encephalitis is well developed physically and has a normal personality but has difficulty of motility. It learned to run between the ages of 1½ and 2 years; since the age of 2½ it has suffered with attacks of suppuration of the middle ear every fall; speech began between the ages of 2 and 3 years, but not until tonsillectomy was performed. The father and his parents are extremely nervous and irritable.

In none of the 124 cases did there occur more than one case in any one family. In this connection it is interesting that Stern and Grote, who had occasion to observe 450 cases of encephalitis, found only three cases of encephalitis in more than one member of the same family.

From a geographic point of view, there is nothing unusual about the occurrence of the disease. Aside from the abortive cases and the mild cases which were characterized only by changes in character and difficult social adjustment, there is nothing unusual about the course of the disease. The paper is concluded with a plea for the establishment of an institution in which the patients with chronic cases could be treated clinically as well as pedagogically.

LITTLE'S DISEASE IN SISTERS AND BROTHERS AND IN TWINS. GEORG STIEFLER, J. f. Psychol. u. Neurol. **37**:362, 1928.

The paper deals with three observations on familial Little's disease. Observation 1: A sister and brother, aged 15 and 13 years, respectively, were both prematurely born and showed congenital spastic paraparesis, dysarthria, strabismus and feeblemindedness. Observation 2: Three sisters, aged 13, 15 and 23 years, respectively, two of whom were prematurely born, and one had a delayed and difficult birth, all had congenital diplegia, cranial anomalies, speech disturbances, strabismus and imbecility; one of them also had choreo-athetotic movements. All patients thus far described showed evidences of hereditary syphilis. Observation 3: Two prematurely born twin brothers showed general congenital muscular rigidity, speech disturbances and imbecility; their mother was also an imbecile.

Stiefler emphasizes the desirability of limiting the term Little's disease to a group of cases of infantile cerebral palsies which are characterized by: abnormal birth (premature delayed or difficult); congenital cerebral maldevelopment (regressive tendencies); paraplegia or diplegia with cerebral manifestations and muscular rigidity preponderating over the paretic phenomena. Syphilis plays an important rôle in Little's disease, especially in the familial forms. Genuine familial Little's disease is rare, but Little's disease in twins is unusually so.

THYMOGENOUS CAPILLARY ATONY AS A CAUSE OF CEREBRAL DISTURBANCES. CARL WICHURA, J. f. Psychol. u. Neurol. **37**:401, 1928.

A well developed, obese farmer, aged 55, with unusually large extremities, after an entire winter's inactivity, became more obese and began to have periods during which he suffered from headaches, depression, anxiety, insomnia, muscular contractions, generalized "sticking" pains and paralyses involving one of his upper extremities and half the tongue. These symptoms came on periodically and would last for weeks at a time. At the beginning of the spring he became active again and after having been subjected to a "reducing" diet began to lose weight and regained his usual physical and mental health. As the symptoms began to regress, he was noted to have developed a marked atony of the capillaries at the margins of the nails. With complete recovery this phenomenon had also entirely disappeared. The only organic observation in the case was a marked polycythemia.

According to Wichura, this case seems to confirm Westphal's theory of the angiospastic origin of apoplexies and may serve as a contribution to the knowledge of the apoplexies sine materia.

The cerebral manifestations presented by the patient could justify the assumption that one was dealing here with a certain amount of increased intracranial pressure, whereas the mental symptoms were extremely suggestive of a transitory Korsakoff syndrome. Fever, uremia, toxic or expanding intracranial lesions could definitely be excluded as causative factors. The rapid disappearance of the nervous symptoms, as well as the changes in the blood picture following the general improvement, would also speak against the polycythemia as an etiologic agent. A study of the blood picture was also suggestive that one was dealing with a symptomatic polycythemia which, according to Nägeli, must be regarded as a secondary manifestation of disturbances of the endocrines. There was nothing in the history to point to the possibility of a transitory polycythemia following poisoning by phosphorus, carbon monoxide or trichinosis, nor was there any evidence of tuberculosis of the spleen.

From the point of view of constitution it was noteworthy that the patient's family consisted of strong, long-lived, tall and obese persons, although there was some familial tendency to tuberculosis. Except for the unusually large extremities his physical development was normal. There was no evidence of defective development or hypofunction of the genitalia or of the thyroid. The disproportion in the size of the body and limbs with the obesity and vascular atony could not be attributed to any hypophyseal disturbance, because closer study revealed that the skull was normal; there were no abnormal distribution of the body fat or

disturbances in the urinary excretion. Furthermore, although the patient's mood could be interpreted as a sequel to cerebral circulatory disturbances as well as to hypophyseal dysfunction, the latter would have to be in the nature of a hyperfunction of the anterior lobe to account for the large growth, and of a hypofunction of the middle and posterior lobes to account for the obesity. To explain the entire clinical picture one would also have to find some reason why the second tonus mobilizer of the blood vessels — the suprarenals — temporarily failed to perform their function. All in all, any attempt to attribute all the clinical phenomena in this case to an actual disturbance of the hypophysis would encounter too many objections.

Wichura believes that an involvement of the thymus would best explain the entire clinical picture. According to Biedl, hypofunction of this gland is characterized by unusual body height with very long extremities and a relatively short trunk, a well developed panniculus adiposus and a tendency to tuberculosis — all of which features were present in this case. The thymic involvement may also have been a factor in the production of the vagatonia and, as the opposite to the two tonus maintaining agents (posterior lobe of the hypophysis and suprarenals), to the vascular atony. The fact that lymphatic glands were not demonstrable clinically in the patient may have been due to their disappearance before the patient reached his present age, or to an absence of the lymphatic component of his thymic constitution. Of interest in this connection also are the high lymphocytic count (34 per cent) and the high thymus figures obtained by Abderhalden's interferometric examination, even though no enlargement of the thymus could be made out clinically. Retrogression of gonadal activity, lack of muscular effort, obesity due to overeating and the time of the year during which the patient became ill (winter) were probably additional factors in the thymus dysfunction. The latter was probably a transitory phenomenon, because as soon as the patient's weight was reduced and with the onset of warm weather he was subjected to cooling, tonic carbonated baths during which increased muscular activity was encouraged, his symptoms improved rapidly.

The capillary atony, as observed microscopically, exceeded in intensity that of any other case observed by the author in thousands of patients subjected to such examination during the past ten years. One glance under the microscope was at once suggestive that it was the capillary atony that was at the basis of the patient's various circulatory disturbances. Wichura believes that all cerebral vessels were affected, and the more pronounced paretic phenomena he attributes to quantitative differences in the circulatory disturbances of the cerebral cortex. What effect the chemicotoxic changes of the blood and body juices had on the cerebral manifestations must, in the present state of knowledge, still remain an open question.

KESCHNER, New York.

MENINGEAL PERMEABILITY AND DIAGNOSIS OF MENINGITIS IN CHILDHOOD. HERMANN ESSELBRUGGE, Monatschr. f. Kinderh. **43**:45 (March) 1929.

It has been found that 0.03 Gm. per kilogram of body weight of a 20 per cent solution of uranium, injected intramuscularly, will be excreted into the spinal fluid in persons with meningitis. In cases in which meningitis is present, if a lumbar puncture is made three hours after the injection, the spinal fluid will show marked fluorescence. The presence of colorless spinal fluid rules out meningitis. The author tried this test in a number of cases and found it of considerable value, particularly in a case of poliomyelitis which greatly simulated meningitis.

In no case was there any injury to the patients, although they often appeared icteric for from two to nine hours.

The increased permeability of the membranes to uranium is probably caused by the fact that the uranium is bound to the blood protein.

GERSTLEY, Chicago.

MENINGITIS IN CHILDREN CAUSED BY KOCH-WEEKS' BACILLI. H. MEYER and R. STEINERT, München. med. Wchnschr. **75**:945, 1928.

The symptoms, the clinical progress and the results of bacteriologic studies of three children with meningitis caused by Koch-Weeks' bacilli are reported. None recovered, and the results of the postmortem examination of the brain of two are given. Both had a marked suppurative meningitis.

E. F. HIRSCH.

ENCEPHALOGRAPHY IN TUMORS OF THE POSTERIOR FOSSA. FRITZ EUGEN FLÜGEL, Ztschr. f. d. ges. Neurol. u. Psychiat. **115**:551 (July) 1928.

Tumors of the posterior fossa often give an indistinct clinical picture; hence, encephalography is of value. In addition to the ventricular dilatation which accompanies these lesions, Jüngling pointed out that there is another characteristic which consists of a shadow slighter on the side of the tumor than on the opposite side. This is due to a shortening of the posterior horn owing to pressure by the tumor from below. Air was introduced in Flügel's cases by means of ventricular puncture. Four views were taken: one anteroposterior, one posteroanterior and two lateral views. Flügel found in two cases that the posterior bone is compressed on the side of the tumor in the posterior fossa, and this compression is shown by a shortening of the posterior bone on that side.

ALPERS, Philadelphia.

PATHOGENESIS OF HYDROCEPHALUS. ARVID LINDAU, Arch. path. et microbiol. Scandinav. **5**:25, 1928.

A summary is given of the formation, circulation and absorption of the cerebrospinal fluid (chiefly based on American investigations). On this basis, the nature and pathogenesis of hydrocephalus are discussed. Hydrocephalus is not a disease but a symptom of an occlusion in the circulating system of the cerebrospinal fluid. The author's method of injection of a dye at autopsy into the lateral ventricles to determine the site of the obstruction is described. This method may be employed as well in communicating as in noncommunicating hydrocephalus. Fifteen personally observed cases of hydrocephalus, analyzed according to Dandy's principles, are presented; among them is a case of external hydrocephalus.

[ARCH. PATH.]

A CASE OF EPIDEMIC ENCEPHALITIS POSTVACCINALIS. E. DE VRIES, Nederl. Tijdschr. v. Geneesk. **72**:5081, 1928.

A Chinese boy, aged 6 weeks, became ill three days after vaccination and was taken to the Neurologic Clinic of the Peking Union Medical College with symptoms of encephalitis: somnolence, vomiting, conjugate deviations of the eyes and convulsions. He had repeated attacks of apnea and died in high fever after a fortnight. Examination of the brain demonstrated a nonhemorrhagic encephalitis, principally localized in the thalamus and the substantia nigra, and less in the nuclei of the eye muscles, the pons and the oblongata. The spinal cord and the cerebral cortex were totally intact, with the exception of an encephalomalacic lesion probably caused by vascular spasm. Microscopically, perivascular infiltration with lymphocytes and some plasma cells and a diffuse increase of glia fissure were found next to the degeneration of the ganglion cells. There was no perivascular demyelinization.

All the symptoms and manifestations in this case, therefore, are typical of epidemic encephalitis. In the author's opinion, in this case there was an accidental coincidence of vaccination and epidemic encephalitis. The fact that the picture of the encephalitis was disturbed neither clinically nor anatomically by the vaccination gives important support to the conception that the encephalitis postvaccinalis which occurs in Europe and principally in Holland forms a separate group, or that the difference between postvaccinal and common epidemic encephalitis is founded on a difference in the virus.

VAN CREVELD, Amsterdam.

AMYOTONIA CONGENITA AND SPINAL MUSCULAR ATROPHY OF WERDRIG-HOFFMANN IN ONE FAMILY. T. HALBERTSMA, Nederl. Tijdschr. v. Geneesk. **72**:6180, 1928.

In recent years there has been a tendency in the literature to accept the view that amyotonia congenita and spinal muscular atrophy are identical. In this connection, the communication of the author is of value. He describes a family in which, successively, three children were born who after some time appeared to be suffering from or began to suffer from hypotonia and weak paralysis of the muscles. There was a loss of the reflexes, and the child's life was threatened by pneumonia. In the first child the diagnosis of amyotonia congenita and in the two others that of spinal muscular atrophy were made.

As both diseases are rare and the chance that they occur successively in two succeeding children in one family is small, it is the author's opinion that his observation points to an identity between them.

VAN CREVELD, Amsterdam.

TEMPORARY LOSS OF EYESIGHT DUE TO PRESSURE OF THE CEREBROSPINAL FLUID. S. KAMIOKA, J. Pediat. (Tokyo), Jan. 20, 1929, no. 344, p. 98.

The author reports the case of a boy, aged 3⅓ years, who suddenly developed slight ataxia followed by an almost complete loss of eyesight together with pain in the legs, but no fever or other symptoms of acute illness. The pupillary reflexes to light were diminished but in accommodation were normal. The urine was normal, as was the blood picture. The lumbar puncture showed a pressure of 200 mm. of mercury, with 24 cells, all lymphocytes, and the globulin, uranin and bacterial examination negative. The total nitrogen was 32.2 and the residual nitrogen, 29.4. The sugar was 0.05 per cent. The subsequent lumbar punctures restored the eyesight, and the patient was discharged in good condition. The author does not make a diagnosis of the case, but he thinks that this is an afebrile type of encephalitis.

URANIN TEST AS AN AID TO THE DIAGNOSIS OF MENINGITIS. SHIGERU HAMANO, J. Pediat. (Tokyo), Jan. 20, 1929, no. 344, p. 103.

The author used 0.02 Gm. of uranin per kilogram of body weight in infants under 1 year of age and 0.03 Gm. for older children. He employed this test in eighteen cases of definitely diagnosed meningitis, and obtained fourteen positive and four negative results. He made the same test in four cases of encephalitis, and one case each of infantile convulsion, neurosis, hydrocephalus, abscess of the brain, and meningismus which occurred during the course of empyema, and obtained negative results in all cases. He states that the test gives positive results only in cases of well advanced meningitis.

KATO, Los Angeles.

Diseases of the Eye

CONGENITAL BILATERAL MICROPHTHALMOS ACCOMPANIED BY OTHER MALFORMATIONS OF THE BODY. A. M. YUDKIN, Am. J. Ophth. **11**:128, 1928.

The other malformations present were: a malformed heart on the right side, an undescended left testicle, bilateral talipes calcaneovalgus, supernumerary and deformed fingers, a congenital defect in the diaphragm with herniation of the stomach and spleen into the thoracic cavity, and a double ureter. The child died when 35 days old. The author gave the following summary and conclusions: The case seems to be that of a simple microphthalmos. It was probably produced by the presence of mesoblastic tissue and persistent embryonic vasculature in the vitreous cavity. The nourishment furnished from this source was beneficial only to the retina, which grew prolifically.

This sustains the contention of von Hippel that the expansion of the globe depended on the normal inhibition of fluid by the vitreous. The microscopic picture

of the eye indicates that the course of further growth of the vitreous was probably altered by the underdevelopment of the ciliary body and its processes, hyperplasia of retinal tissue and lack of choroidal vascularization. It was probably this arrest of development which was responsible for the microphthalmos. It was surmised from the presence of the Wintersteiner retinal rosets that they were not pathognomonic of a malignant condition, as often contended. [ARCH. PATH.]

CONGENITAL ABSENCE OF ABDUCTION. A. WILDE, Am. J. Ophth. **11**:780 (Oct.) 1928.

The author reports the case of a girl, seen at the age of 7 years, who was unable to abduct either eye. This condition was first observed by the parents when the patient was 4 years of age. As far as could be determined, it was congenital. When the patient looked to the right, the right eye did not move any appreciable distance beyond the midline, while there was adduction of the left eye. Similarly, when she looked to the left the reverse was true: the left eye remained in the midline and the right eye was adducted. All other neurologic and ophthalmoscopic observations were reported as normal.

FERGUSON, Philadelphia.

NEVUS OF THE BULBAR CONJUNCTIVA. F. H. RODIN and E. M. HALL, Am. J. Ophth. **12**:24 (Jan.) 1929.

In the case of a boy, aged 6, who was first seen in August, 1927, the mother a year previously had noticed a small brown spot on the white of the right eye, which had increased in size and recently had become surrounded by a red zone. Examination disclosed an irregular brown area about 2 by 3 mm. on the bulbar conjunctiva of the right eye, 7 mm. from the limbus. It was surrounded by a hyperemic zone about 2 mm. wide; it was not elevated and was freely movable. The growth was removed, and showed no signs of recurrence a year later. The histologic diagnosis was: a pigmented nevus of the conjunctiva.

The twelve cases reported in the literature during 1925 and 1926 are summarized; the tendency of these growths to become malignant is emphasized.

W. S. REESE.

SERIOUS HEMORRHAGE FROM THE CONJUNCTIVA IN AN INFANT FOLLOWING THE INSTILLATION OF SILVER NITRATE SOLUTION. J. G. F. HEAL, Brit. J. Ophth. **12**:33 (Jan.) 1928.

A 15 per cent solution of nitrate of silver had been instilled into the eyes of a new-born infant five times in thirty-four hours, as ordered by the medical attendant. The bleeding which was mostly from the left eye could not be checked by the usual means. The child, who was growing weak, was anesthetized for examination. The conjunctiva of the upper lid showed an extensive raw area. The bleeding points, which were chiefly in the region of the subtarsal furrow, were sealed with a heated probe.

ON PSEUDOGLAUCOMA. A. FUCHS, Brit. J. Ophth. **12**:65, 1928.

The author refers to a previous paper in the *American Journal of Ophthalmology* in which some anomalies which might be mistaken for a glaucomatous excavation were pointed out, such as: an oblique insertion of the optic nerve; a large physiologic cupping; branching of the central vessels behind the lamina cribosa, so that their individual branches emerge only at the margin of the papilla, and a congenital coloboma of the papilla if a circumscribed depression of its surface has produced a pitlike cupping.

The author records the occurrence of a congenital pit coexisting with a glaucomatous excavation. The pit admits of a twofold interpretation. It may be a deeper part of the general glaucomatous excavation, a less resistant part of

the lamina cribosa which yields to the intra-ocular tension more than the rest. This would be found only in glaucoma of long standing with extreme hypertonia. On the other hand, there may be a simple coincidence of glaucoma and congenital pitting.

He also reports a case of colobomatous excavation simulating glaucoma. Reduced vision and the aspect of the papilla indicated glaucoma but the fact that the papilla was larger on the left proved the case to be a congenital colobomatous excavation. There was a greatly enlarged blind spot extending along the horizontal meridian. One year later the picture was unchanged. A similar case in a girl, aged 12½ years, is described.

As a condition resembling inflammatory glaucoma, a case of angiectasia of the eyeball is cited. A boy, aged 14 years, complained of unsteady and failing vision. The conjunctiva of the lids and transitional folds exhibited small vessels between the larger ones, with occasional minute varicosities. There were also delicate traction cicatrices. On the globe were numerous vessels of unusual breadth and tortuousity running backward from the limbus. The dark color showed them to be veins. To a lesser degree, an analogous change existed also in the vascular system of the retina, a macular vessel being enlarged and tortuous within the papilla. All the symptoms of glaucoma were absent.

The author cites two other cases from the literature and one case communicated to him by his father. The condition appears not to be congenital.

RACE, SEX AND ENVIRONMENT IN THE DEVELOPMENT OF MYOPIA. PRELIMINARY COMMUNICATION. A. SOURASKY, Brit. J. Ophth. **12**:107 (April) 1928.

This study was conducted among the Jewish and non-Jewish population in the East End of London. The author points out that the Jewish children were almost all born in England. In the vast majority of cases, their parents are of Polish and Russian origin. They are brought up much as the children of the non-Jewish population, except that the boys who attend the elementary day school also attend classes for the study of Hebrew several evenings each week under conditions which are by no means ideal.

He gives the following summary of his observations:

1. The incidence of visual defects among Jewish boys in the East End is more than 40 per cent — double that of the non-Jewish boys.

2. This heavy incidence of defects among Jewish boys is stationary all through their school life; it is practically no heavier at the age of 14 than at 7.

3. The incidence of the defects, therefore, is not increased with school life, and apparently is not produced by the excessive amount of work done by Jewish boys.

4. Comparative analysis of the refractive errors seen among the defectives of the Jewish and non-Jewish children reveals little difference in the distribution of errors, apart from a rather higher incidence of myopia and of low hypermetropia among the Jewish children.

5. There is little difference in the percentage of cases of myopia in the early years of school life (from 5 to 9) in the two groups. The greater incidence of myopia among Jewish children becomes marked in the later years (from 10 to 14).

6. It is argued that the greater increase of myopia in the later years among Jewish children is not the result of excessive close work, but of the greater incidence of low hypermetropia among the young Jewish children.

7. An attempt is made to establish this contention mathematically.

8. When the analyses are carried further to bring out any distinction in the increase in the number of cases of myopia among Jewish boys as compared with that among girls, it is found that the increase is decidedly greater among the boys (who do much more close work).

9. However, the same is seen to be true of the non-Jewish boys (who do not do an excessive amount of close work) as compared with the non-Jewish girls.

10. It is suggested, therefore, that there is a sex determined factor which controls the growth of the eye.

11. The excessive incidence of myopia among Jewish boys is explained by the racial factor of the great prevalence of low hypermetropia and the sex determined (and nonracial) factor which allows for a greater or longer development of the length of the eye.

BILATERAL CYSTS OF THE CORNEA. L. W. FOX, Brit. J. Ophth. **12**:249 (May) 1928.

A girl, about 11 years of age, had a double advancement of the external recti for convergent strabismus performed by another surgeon, with a partial improvement of the squint.

At the site of the anchorage of the advancement in the left eye, there was a V-shaped separation of the sclera, at the bottom of which the pigment of the choroid could be seen. The separation extended into the cornea giving it a steamlike aspect. In the right eye, a similar condition was much less marked.

The biomicroscope disclosed that the separation in the cornea was a cyst lying between Bowman's and Descemet's membranes. On either side of the V, blood vessels could be seen.

As the condition progressed, a keratome was passed into the cornea at the upper margin, on the temporal side of the steamy area. The point of the instrument entered the cyst. The lower margin of the steamy V was divided by scissors to cut off the blood supply. The edges of the wound were cauterized with trichloracetic acid. Later, a small white isolated scar between the center and margin of the cornea could be made out. The hernia of the ciliary body subsided and the scleral opening closed.

THE GROWTH OF THE EYE AND THE DEVELOPMENT OF MYOPIA: A STUDY IN THE CHANGES OF REFRACTION DURING THE SCHOOL PERIOD. A. SOURASKY, Brit. J. Ophth. **12**:625 (Dec.) 1928.

The material used for this investigation consists of the "follow up" records of the school clinic of the Tottenham Urban District Council. Some of the records date back to 1915. The children were between the ages of 5 and 14. The refraction was done by one person. Retinoscopy was done under the influence of scopolamine. The selected material came from 1,242 eyes. These were divided into two groups, one containing 395 cases of hyperopia, including hyperopic astigmatism, and another containing 226 cases of myopia, including myopic astigmatism, mixed astigmatism and other cases containing a myopic element.

Under "no change" were included all cases which did not show change in refraction or a change of $+0.5$ or -0.5. In astigmatism, when axes developed at unequal rates, any difference up to and including $+0.5$ or -0.5 was ignored, and when there was a difference of from 0.5 to 1 it was divided and added to each axis. When the difference was greater than 1 diopter, the case was considered irregular.

The author's summary is as follows:

When traced for a period of from three to five years, about 65 per cent of the patients with hypermetropia did not show any reduction. Of the remaining cases, a reduction of more than 1 diopter was seen in only a few.

Rather similar proportions were obtained for the smaller number of cases followed up for from six to eight years, as far as the percentage of cases which did not show reduction is concerned; for those cases that do show reduction, the tendency is for the reduction to be rather heavier.

In all probability, these considerations apply equally to all degrees of hypermetropia, whether near the emmetropic margin or more than 6 diopters.

About 35 per cent of cases of myopia appear to be stationary when followed up for between three and five years, and about 15 per cent show an increase of

not more than 1 diopter; it is only in the remaining 50 per cent that the progression is seen which one associates with all cases of myopia.

Unlike the conditions seen among patients with hypermetropia, the different degrees of myopia appear to behave in a different manner. Thus, low myopia seems to tend more toward progression than medium and high myopia, and mixed astigmatism.

A consideration of cases of abnormal development reveals that some cases of hypermetropia developed more on the lines of the rapid progression seen in myopia than on the relatively stationary condition or slow progression usually obtained in hypermetropia. Much of the evidence brought forward is concerned with the unequal development seen in the two eyes of one person.

Similar unequal development is shown to exist among patients with myopia.

It is concluded that not only may there be a varying rate at which the eyes of different persons develop, but also that the two eyes in the same person may develop at a different rate, and, incidentally, the congenital condition of most cases of anisometropia is questioned.

Mainly in view of the fact that there are: (1) some cases of hypermetropia changing as rapidly as those of myopia; (2) some cases of myopia remaining as stationary as those of hypertropia, and (3) symmetrical eyes progressing unequally, it is argued that the refractive condition of an eye has nothing to do with the tendency to progression. This tendency is regarded as an abnormal state supervening as readily in the hypermetropic as in the myopic eye, and may affect one eye only. That this tendency should be more often seen in myopia is only to be expected, as it induces a myopia when this condition has not existed before. Myopia is the result, not the cause, of progression.

Cases are quoted to illustrate how hypermetropia that has been stationary for years suddenly diminishes, without going on to myopia, because of a sufficient hypermetropic reserve.

Of the behavior of this disorder which induces elongation of the globe, it is pointed out that it has an evolutionary course, beginning at some period of childhood, and persisting through adolescence (progressive myopia), though it may become arrested at an earlier age (stationary myopia in children), or go on through adult life (malignant myopia). (The usual age of the onset of this disorder is probably somewhere from 12 to 14 years.)

A passing suggestion is made as to the nature of this disorder.

During the school period, the growth of the eye has little effect on its refractive condition.

W. ZENTMAYER.

MYCOSIS OF THE PALPEBRAL CONJUNCTIVA. G. SCALZITTI, Ann. di ottal. e clin. ocul. **56**:1023 (Nov.) 1928.

A boy, aged 11, showed a marked swelling of one upper lid which had been present for six months. Granulations had been excised three times but had recurred each time. Two yellow nodules the size of a pinhead were present just inside the border of the lid, surrounded by numerous smaller white points in an area of infiltrated conjunctiva. Wassermann and Pirquet reactions were negative. The globe was not affected. A portion of the conjunctiva, removed for section, showed a nodule resembling a tubercle with threads staining with hematoxylin resembling those of a fungus. A fragment inoculated into the anterior chamber of a rabbit produced a small nodule of the iris which was still present after five months. Ten injections of iodized oil caused the lesions to clear up entirely. The type of fungus could not be determined from the sections, and cultures evidently were not made. The clinical resemblance to Pereyra's case of streptothricosis of the conjunctiva is noted. A bibliography, a photograph and a photomicrograph are included.

S. R. GIFFORD.

THE RELATION BETWEEN CONGENITAL CATARACT AND CHANGES IN THE NEUROVEGETATIVE APPARATUS. C. GIANUANTONI, Ann. di total. e clin. ocul. **56**:1063 (Dec.) 1928.

The importance of proper equilibrium between the sympathetic and parasympathetic nervous systems in the development of the organism is discussed. Any disturbance of this balance during development, or in that of the mother during fetal life, may give rise to anomalies in the growth of various organs. The author investigated the neurovegetative system in twelve cases of congenital cataract. Pharmacodynamic tests were performed, inoculations of 5 per cent morphia and 1 per cent epinephrine being made according to the Pirquet technic. The reflexes giving information about the vegetative nervous system, such as the oculocardiac reflex and the appearance of dermographia, were recorded, and the blood calcium was determined.

In none of the cases was any evidence found of endocrine dysfunction. Seven cases showed by their reflexes a hyperfunction of the parasympathetic system, while five showed no predominance of either system. The Wassermann reaction was negative in all patients. The blood picture and blood calcium in all cases were within normal limits, and roentgenograms of the sella showed no marked abnormalities. The skin tests with morphia and epinephrine varied without showing any constant relation to the other observations. No evidence of rachitis or tetany was found. Thus the only evidence that vegetative dysfunction plays a part in causing congenital cataract was the evidence of vagotonia in seven cases, the importance of which, the author concludes, will depend on further observations in a large group of cases. A bibliography is included.

CATARACT, TETANY AND DWARFISM. P. SAINTON and G. RENAUD, Arch. d'opht. **45**:391 (June) 1928.

The picture of tetanic cataract, as Weill and Nordmann have described it in their research on cataract and its relations to general pathology, is classic.

The authors call attention to the cases already reported and the experimental evidence which has been obtained.

They then report the case of a patient, aged 47, 128 cm. in height and weighing 38 Kg. He had first lost the sight of his right eye from cataract which was operated on with a good visual result. Although his left eye failed later in a similar manner, he came under observation because of symptoms of tetany. The cataract in this left eye was so far advanced that it was difficult to determine its variety.

He had been subject to seasonal attacks, which occurred usually from January to March, since he was 12 years of age. He had the usual clinical signs of tetany. X-ray pictures demonstrated changes in the long bones somewhat like those found in rickets.

It seems probable that in this case disease of the parathyroid glands is chiefly responsible for the whole clinical picture.

S. B. MARLOW.

THE FREQUENCY OF CONGENITAL ANOMALIES OF COLOR SENSE IN BOYS AND GIRLS. P. VON PLANTA, Arch. f. Ophth. **120**:253 (April) 1928.

School children were examined with the common color tests and with the anomaloscope for anomalies. Of 2,000 boys, 7.95 per cent were found with a defective sense of color; of 3,000 girls, only 0.43 per cent. The color test, which was devised by Ishihara in 1917, detected all the cases of a defective sense of color, and is more reliable then any of the other color tests. As to reliability and certainty the tests can be put in the following order: Schaaff's tableaux mosaiques, Stilling's pseudoisochromatic plates, Cohn's plate and Nagel's plates. Nagel's plates were found to be complicated, fatiguing and unreliable; about 15 per cent of the patients with a defective sense of color stood the test.

P. KRONFELD.

ON THE OXIDATION MECHANISM OF THE CRYSTALLINE LENS. GUNNAR AHLGREN, Acta ophth. **5**:1, 1927.

Ahlgren investigated the methylene blue metabolism of the lens tissue by a method introduced by Thunberg in the study of other tissue. He noted that the oxido-reduction power of the lens is considerably diminished on exposure to a temperature of — 80 F. and that it is merely abated when subjected to a temperature of + 60 F. Because of these changes in the oxido-reduction power of the lens he believes that the tissue has an oxidation enzyme of the type called dehydrogenosis which plays an important part in the oxidation mechanism of the lens. Dehydrogenosis affecting the oxidation of fumaric, malic, glycerophosphoric, lactic, citric, acetic and the amino-acids — alanine and valine — has been found to exist in the lens. In a similar test, however, succino-dehydrogenase, which has been found in all other tissues, is absent in the lenticular mass. To a certain extent, therefore, the metabolism in the lens follows a different path from that of muscle and other tissue. The lens cortex shows a greater oxidation intensity than the lens nucleus. Ahlgren also noted that the oxidation in the lens cortex of some thyroidectomized rabbits is increased from the subnormal intensity by the administration of suitable concentrations of thyroxin. High concentrations of thyroxin retard the oxidation intensity of normal and thyroprive lens cortex.

THE QUESTION OF ENDOCRINE ETIOLOGY OF JUVENILE CATARACTS. V. GRÖNHOLM, Acta ophth. **5**:166, 1927.

From an analysis of five cases of bilateral juvenile cataracts which were accompanied by some manifestation of disturbed internal secretion and a review of the literature on the subject of cataract formation in endocrine disturbance, Grönholm classifies the cases into the following groups: In the first group he places the lenticular opacities which are accompanied by disturbed internal secretion, such as diabetic cataract due to hypofunction of the pancreas; tetany cataract produced by hypofunction of the parathyroid glands; myotony cataract seen often in hypofunction of the thyroid and parathyroid glands; acromegaly cataract due to hyperactivity of the anterior lobe of the hypophysis; diabetes insipidus cataract produced by hyperfunction of the pars intermedia of the hypophysis, and pluriglandular cataract due to a dysfunction of internal secretion. In the second group are the cases which show no signs of disturbance of the internal secreting glands. These include cataracts which are produced by the introduction of toxic substance into the ocular tissue through the blood stream. If the toxin disturbs the internal secreting gland, and these in turn the lens, the cases are to be classified in the first group.

A. M. YUDKIN.

Diseases of the Ear, Nose and Throat

THE ETIOLOGY AND THE ETIOLOGICAL TREATMENT OF "PLAUT VINCENT'S ANGINA." P. MANGABEIRA-ALBERNAZ, Laryngoscope **39**:1, 1928.

The disease commonly called Vincent's angina is a fusospirochetosis and is caused by the association of the fusiform bacillus of Le Dantec with the spirochete of Vincent. The important factor to be kept in mind in considering the etiology is that the lesions are produced by the joint action of the two organisms, neither being able alone to bring about the morbid character of the condition. It has been demonstrated by careful studies in pathologic anatomy that the spirochete penetrates deeply into the tissues, and in order to reach it therapeutically it is evident that the remedy used should fulfil special conditions which the author believes have usually been ignored. The various requisites to be considered in the choice of a remedy include the employment of one that is readily absorbed by the tissue in order to penetrate to the deeper layers. It should be antiseptically active for an appreciable time; it should be neither caustic nor destructive, but, at the same time, it should have a dissolvent action on the necrotic tissue characteristic of the lesion. Its antiseptic action should be specific on one or the other component of the symbiosis, for if one of these is eliminated the symbiosis is destroyed.

These various conditions have been found to be present in a high degree in only two series of substances: the bismuth substances and the arsenobenzenes. The author has carried on extensive work with the bismuth salts in the treatment for Vincent's angina and finds that it has many advantages over the arsenobenzenes, among these being that it is less toxic, more powerful, more economical and immediately and certainly sedative in allaying the characteristic pain. The treatment usually employed consists in the daily local application to the ulcerated area of a salve emulsion of bismuth tartrate of 30 per cent strength. This is supplemented with the gargling of any mild antiseptic every two or three hours. The author finds that the severe cases rarely require more than three treatments.

LATENT DISEASE OF THE MAXILLARY SINUS. WILLIAM MITHOEFER, Laryngoscope **39**:29, 1928.

Pathologic changes in the maxillary sinus have often remained unrecognized because of the lack of symptoms referable to the nose. The normal mucous membrane lining the antrum becomes, with pathologic changes, an edematous one of low vitality, with a predisposition to recurrent infections, and may even become an atrophic pyogenic membrane after repeated inflammatory attacks. Close observation has disclosed the fact that a toxemia may be caused as readily by a low grade infection without demonstrable pus within a bony cavity as it is by a purulent infection. Consequently, the author believes that in uncovering a hidden focus of infection within an antrum, a definite and important step is made in the practice of preventive medicine.

The diagnosis of these latent sinus infections is frequently difficult and requires extremely careful observation and study. Except for the presence of repeated vasomotor disturbances of the nasal mucosa, few, if any, local changes are found in the nose. The presence of a hyperplastic ethmoiditis, a protrusion of the membranous middle meatal wall of the antrum or a polypoid change of the inferior turbinal, especially in its posterior third, should make one suspicious of the possible presence of an antrum infection. The history of repeated colds and of a persistent postnasal discharge of mucus are also factors to be considered. Latent antrum disease is frequently responsible for many of the aggravating symptoms of hayfever, as evidenced by the fact that irrigation of the antrum with hypertonic saline solution during the attack will often bring immediate relief. The instillation of iodized oil into the antrum, followed by a skiagram to denote any possible filling defect, is a valuable aid in determining the presence of these latent conditions. The skiagram, without the aid of the iodized oil, is not conclusive, especially in those cases which reveal negative observations but arouse suspicion clinically. The author has repeatedly found marked hyperplasia in deep recesses of the antrum in patients in whom a clear skiagram and negative lavage were obtained. Lavage may often be negative. Especially is this true when there is good drainage because of a large accessory ostium. Close follow-up of all cases of acute antrum infection is extremely important. Even though the pus disappears after several irrigations, a low grade latent infection may linger, which may become a definite focus.

The importance of recognizing these latent and obscure infections before or at the time of doing an intranasal operation is strongly emphasized. If an antrum infection is overlooked at the time of an ethmoid exenteration, the end-results may be discouraging to both the patient and the surgeon. In such instances, it is often impossible to persuade the patient to undergo a second operation. The method of approach in dealing with these latent antrum conditions may be either intranasal or radical, depending on the individual case. Intranasal procedures frequently are all that are required.

SNAPP, Grand Rapids, Mich.

SUDDEN DEATH DUE TO OCCLUSION OF THE LARYNX BY ASCARIS LUMBRICOIDES. M. B. DUNCAN DIXEY, Edinburgh M. J. **36**:111 (Feb.) 1929.

A negro girl, aged 8½ years, suddenly fell forward on her face during strenuous exercise, gasped for breath and became unconscious. She died within a few

minutes. The postmortem examination on this child, who had been healthy and well nourished, showed froth in the nose and mouth, and a congestion of the conjunctivae. The thoracic and abdominal viscera were congested. When the tongue and larynx were removed, two large round worms were seen protruding from the larynx, one partially curled up within it, so that the entire larynx was occluded by the two worms and respiration was prevented. The trachea and bronchi were full of froth, the walls congested and the vessels filled with dark blood. The right side of heart was dilated, the left side empty. A worm was also found in the stomach and two others in the small intestine. The author concludes that these large adult worms had ascended from the stomach and had been inspired due to the violent respiration caused by the particular exercise which the child was performing at the time. Death was due to asphyxia.

NEFF, Kansas City.

NASAL OBSTRUCTION IN CHILDHOOD (PSEUDO-VEGETATIONS). TREATMENT BY DIASTOLIZATION. MARCEL WISNER, Arch. Internat. de laryng., June, 1928, p. 735.

Aside from syphilis, tuberculosis and congenital deformities, nasal obstruction in the very young and in new-born infants is due to adenoid vegetation and the sequelae of the common head cold. After reasonable efforts to free the pharynx of the adenoids, the obstruction many times persists. The author contends that such cases are due to a thickening of the nasal and pharyngeal mucosa and offers diastolization as a relief.

After a reasonable sterilization of the nose by shrinking with epinephrine and the instillation of silver salts over a period of a few days, a soft rubber tube closed at one end and conforming to the curve of the nasal cavity is inserted. A rubber bulb is attached, alternate inflation and deflation of the tube are accomplished and, at the same time, a to and fro movement is executed with the tube.

The purpose of this procedure is not to procure dilatation but to secure stimulation of the nasal mucosa, decongestion of the glandular engorgement and a reflex action of the sphenopalatine ganglion. At the same time, a study should be made of the maternal status, especially in syphilis and tuberculosis.

Three typical cases were reported with favorable results.

ROTH, Chicago.

PRIMARY TUBERCULOSIS OF THE MIDDLE EAR IN INFANTS. M. ZARFL, Virchows Arch. f. path. Anat. **266**:274, 1927.

The author investigated thoroughly four instances of primary tuberculous infection of the middle ear, in which the regional lymph glands were involved, and which presented the picture of a primary complex. Clinically, swelling of the auricular glands appeared first, followed by discharge from the ear, facial paralysis and swelling of the mastoid, with a positive tuberculin reaction in three cases. Pathologic investigation revealed indubitable tuberculous changes with the presence of tubercle bacilli in the structures of the middle ear, and failed to reveal a primary complex in any other part of the body. The infection apparently began in the mucous membrane, and spread to all nearby structures: the labyrinth, middle ear, facial canal, bony walls, etc. Infection probably entered through the eustachian tube. This could take place either during birth, through aspiration of infected amniotic fluid, or afterward from a person with open tuberculosis. In two of these cases the mother, and in one the father, suffered from tuberculosis; in the other, no source of infection could be found.

B. R. LOVETT.

PHARYNGEAL HYPOPHYSIS AND ADENOIDS. M. SLOBODNIK, Ztschr. f. Hals-, Nasen- u. Ohrenh. **22**:165 (Sept. 5) 1928.

Embryogenically, the pharyngeal hypophysis is closely connected with the cerebral hypophysis. The former develops from the outer hypophysis pocket

(Rathke's pocket) and enters through the craniopharyngeal canal in the sphenoidal bone into its permanent place. This portion forms the anterior lobe of the hypophysis (adenohypophysis). The posterior lobe (the neurohypophysis) develops from the base of the midbrain. These two parts are histologically different. Traces of the craniopharyngeal canal rarely persist. The pharyngeal hypophysis is located at the upper posterior border of the vomer, where it meets the sphenoidal bone. In the adult, it measures from 6 to 7 or 9 mm. in length, and is from 0.5 to 1 mm. in thickness. The shape varies. In some cases the basophils are absent in the pharyngeal hypophysis, whereas they are always present in the hypophysis. The chromophil elements surpass the chromophobe elements in the cerebral hypophysis, whereas the relation is just the reverse in the pharyngeal hypophysis. Some authors think that the pharyngeal hypophysis and the cerebral hypophysis have similar functions; others deny this. The author thinks that there is not any absolute relation between the two. In certain instances of tumors of the hypophysis, in cases of dystrophia adiposogenitalis, compensatory changes were not observed in the pharyngeal hypophysis. In a case of tumor of the hypophysis (Christeller) with symptoms of dystrophia adiposogenitalis, the histologic picture of the pharyngeal hypophysis pointed to vicarious hyperfunction. In adenotomy (the author does not perform adenectomy), the pharyngeal hypophysis is not touched. The author suggests that the pharyngeal hypophysis be examined histologically in all necropsies in cases of acromegaly and diseases of the cerebral hypophysis and other endocrine glands.

CONGENITAL DEFECTS OF THE VOMER AND THE DEVELOPMENT OF DEFORMITIES OF THE SEPTUM. KARL M. MENZEL, Ztschr. f. Hals-, Nasen- u. Ohrenh. **22**:181 (Sept. 5) 1928.

According to Gruenwald, a hypoplasia of the sphenoidal part of the septum accompanies a defect of the palate, but it can also occur by itself. Congenital defects of the vomer are reported in the literature. In addition, the defects of the quadrangular cartilage are constituted so that the cartilage, as well as the mucous membrane, are missing, and holes of various sizes can be seen. The opening sometimes is permeable only for a fine probe (Hansemann), but the whole cartilage may be missing. The author describes a case in point in which only the osseous vomer was completely absent, whereas the whole mucous membrane was intact. Gruenwald states that arrested development occurs: (1) by virtue of faulty involution of temporary forms; (2) through lack of normal occlusion; (3) through persistence of early steps of development, and (4) through lack of formative material. The author summarizes that in his case a complete congenital aplasia of the osseous vomer existed and a pronounced vertical deviation of the lamina perpendicularis and of the lamina quadrangularis toward the left side. Furthermore, a completely developed crista lateralis presented itself along a line which otherwise corresponds with the connection between the crista palatina, the lamina quadrangularis and the lamina perpendicularis with the vomer. As the lamina perpendicularis could develop freely downward, it must be assumed that in this instance, the deviation, and especially the crista lateralis, were not caused by external factors influencing their growth but by the embryonic lay which brought about the deviation of the septum and the overgrowth of the lower border of the lamina perpendicularis in the form of a crista lateralis. The case reported permits the conclusion that a number of septums are arranged in the embryonic lay not in the vertical plane. The deviated septum, with its sharp elevations, is surely of embryonic origin in a number of instances.

OTITIS AFTER PACKING OF THE NOSE AND NASOPHARYNX. BACTERIOLOGY AND CLINIC. TIBOR GERMÁN, Ztschr. f. Hals-, Nasen- u. Ohrenh. **22**:191 (Sept. 5) 1928.

The following measures in the nose and nasopharynx may cause acute inflammations of the middle ear: (1) improper irrigation and blowing of the nose; (2) cauterization of the nose; (3) operations in the nasopharynx — especially

adenotomies, which may cause an injury to the tubal ostium or an inflammation of the wound; (4) packing of the nose and of the nasopharynx (after Bellocque) on account of hemorrhage, or prophylactically during operations. Not only mechanical pressure of the soft parts of the tubal ostium but also abnormal secretion, with decomposition of the secretion, are concerned, especially when the packing is left in situ for a long time (Stenger). In the outpatient department of the largest ear clinic in Budapest, only twenty-eight cases were observed from 1919 to 1928. Hartmann reported three cases in 1881. Some authors report the appearance fourteen hours after introduction of the packing (retronasally), whereas Goldberger reported the occurrence on the fifth day after removal of the packing. Most authors (Finder and others) permit the packing to be left in place for only twenty-four hours. In many instances, in spite of all precautions, a complication in the ear may set in. Otto Mayer claims that such a complication is more or less present in every case. He has observed a slight hyperemia of the drum membrane in every case. In such instances, the immediate removal of the packing prevents the development of an otitis. If swelling of the drum membrane accompanies the injection, the removal of the packing is imperative, in Mayer's opinion. The anterior packing of the nose may cause trouble by way of the lymph vessels (von Lenart, Most). The occurrence of tonsillitis is easily explained by the paths of the lymph vessels. The author reports twenty-eight cases in great detail. Retronasal packing was done in six instances. In one patient, a spontaneous perforation of both drum membranes occurred during the first twenty-four hours. If one side of the nose was packed (six cases), the ear on the same side became diseased. In half the cases of retronasal packing, unilateral, in the other half, bilateral, otitis occurred. Of the twenty-eight patients, twenty-three were cured without an operation. The bacteriologic observations were as follows:

Organism	No. Cases
Streptococcus hemolyticus	8
Pneumococcus	3
Streptococcus (Pneumococcus) mucosus	2
Streptococcus viridans	1
Gram-negative *Diplococcus*	1
Streptococcus hemolyticus and *Pneumococcus*	9
Streptococcus hemolyticus, Bacillus pseudodiphtheriae	1
Pneumococcus and *Staphylococcus pyogenes*	1
Pneumococcus and *Micrococcus tetragenus*	1
Pneumococcus and gram-negative *Diplococcus*	1
Staphylococcus pyogenes aureus, Bacillus pseudodiphtheriae and *Diplococcus*	1
	29

In a bilateral infection, pus in the right ear contained *Streptococcus hemolyticus* and *Streptococcus pseudodiphthericus*, whereas on the left side *Pneumococcus* was present. The microbes found in otitis following packing are also normally in the throat, the tube and the nose, especially in the nose and in the throat of patients with hypertrophies, deformed septums, accessory sinus diseases, adenoids, etc. In order to become pathogenic, these microbes must become more virulent. This increase in virulence is greatly favored by packing, especially if it is left in place for a long time, and, most frequently, if it is repeated (Marshik), whereby more favorable conditions are created for the microbes. Clinical symptoms in the form of local inflammatory conditions and, perhaps, rise in temperature bear out this statement. Caldera and Santi proved the injurious influence of packing in experiments on animals, especially when gauze which was not antiseptic was used. This effect was especially evident in an increase of the virulence of old microbes. New microbes could be observed only after packing with sterile gauze. The relative benignity of the otitis caused by packing may be explained by the circumstance that the system can more easily deal with effects of its own microbes, on account of a certain degree of immunity, even if they show increased virulence. In this manner, also, the surprising benignity of the polymicrobic infections may be explained.

THE VALUE OF THE DICK SCARLET FEVER INTRACUTANEOUS TEST FOR LARYNGORHINOLOGIC PATIENTS. KARL M. MENZEL, Ztschr. f. Hals-, Nasen- u. Ohrenh. **22**:233 (Nov. 10) 1928.

1. The Dick test was made on 151 adults who suffered from laryngorhinologic diseases. The scarlet fever toxin of the Vienna serotherapeutic institute did not give a specific intracutaneous reaction. Patients who had had scarlet fever showed the same percentage of positive reactions as those who had not.

2. The assumption was not confirmed that the fact that patients had suffered from angina and peritonsillar abscesses had an influence on the reaction. In the majority of these conditions, the hemolytic streptococcus was found.

3. A former tuberculosis of the lungs did not influence the Dick reaction.

4. The percentage of positive Dick reactions seems to be smaller among patients suffering from peritonsillar abscesses at the time of the test.

5. Frequent repetition of the Dick test on the same person did not show an essential variation in the reaction.

VESSEL CHANGES IN THE PERITONSILLAR TISSUE IN CHRONIC TONSILLITIS. H. C. RIECKE, Ztschr. f. Hals-, Nasen- u. Ohrenh. **22**:261 (Nov. 10) 1928.

The histologic picture of chronic tonsillitis is well known. With the exception of occasional cartilaginous and osseous formations in the peritonsillar tissue, the investigation usually reveals only an increase in the connective tissue, which can be combined with hyalinization of the same, and an obliteration of the vessels. Other changes have not been noted. Laskiewiecz found in chronic tonsillitis an increase of elastic fibers in the connective tissue and an increase of the reticular tissue in the lymph follicles and in the periphery of the same. This is missing in hyperplasia. On the end-vessels, he observed, at unregenerated spots, oval dilatations of the lumen and some sinus-like formations in the lymph. The author reports three cases in which careful histologic examination of the tonsillar and peritonsillar tissue was made. He comes to the conclusion that also in light and uncomplicated cases of angina, thrombophlebitis can occur in the peritonsillar tissue without causing manifest clinical symptoms or general sepsis. Such cases can occur with or without abscesses in the peritonsillar tissue. In one of the cases, peritonsillar abscesses had occurred, and complications in the kidneys and joints had been observed. These could be traced to changes in the blood vessels. The cases described show that a thrombophlebitis may occur which does not always produce threatening symptoms but which can be, if only temporarily, a cryptogenic source of infection, which the organism, as a rule, can combat. Unknown factors may come into play. Why should inflammation progress in one case and not in another? The anatomic structure of the peritonsillar tissue appears to be not without significance. Gaps may be caused by protruding crypts or cones of lymphatic cells, which favor the propagation of a primary infection in the tonsil. Generally, however, the peritonsillar tissue is the first barrier, as can be seen by the increase and cicatricial change of the tissue. It must be emphasized that staining of the elastic membrane is especially adapted to, and imperative in, the detection of these changes. Changes of the vessels can thus be shown which otherwise cannot be found.

In one case, the staining of the elastic membrane showed that at a certain spot of the vein the intima was thickened by connective tissue mixed with fine elastic fibers, whereby the lumen of the vessel was narrowed by one-third. In all three cases there had not been surgical intervention previously, so that the thrombi could not be attributed to incisions. Artefacts are repeatedly caused in small arteries by snaring off of the tonsil at the lower pole. The intima is injured, naturally. On account of the elasticity, the ends of the intima snap back and roll around themselves, whereby a part of the internal elastic membrane splinters off. These pictures are found only near the places of detachment. This may be the reason why bleeding from arteries is observed relatively rarely. The lumen of the arteries is generally closed by this method of occlusion of the stumps.

THE BACTERIOLOGY AND CLINICAL COURSE OF ACUTE MIDDLE EAR SUPPURATIONS, ACUTE MASTOIDITIS AND THEIR COMPLICATIONS. WALTER HESSE, Ztschr. f. Hals-, Nasen- u. Ohrenh. **22**:272 (Jan. 7) 1929.

The course of an acute suppuration of the middle ear and acute mastoiditis can be influenced by very different factors. Examinations were made of 276 patients. A separate picture was furnished by *B. mucosus*. It was especially serious for adults. Wirth was the first to show that *B. mucosus* was agglutinated in all instances by the American pneumococcus III. If there is a suspicion that *B. mucosus* is present, one must insist on the agglutination test, in addition to staining of the capsule and the culture of blood agar soil. The agglutination reveals *B. mucosus* comparatively often during the first and second year but without striking malignancy. The gravity of the infection is dependent not only on the virulence of the microbes, but far more on the resistance of the body. The author has stated that determination of the resistance is uncertain. Yet by certain methods of a bacterioserologic nature (Ruge-Philipp's virulence test), as well as by the faculty of resistance of local cells, one can try to establish it to a certain degree. These investigations show the importance of the local forces of defense which play a part only in acute suppurations of the middle ear and mastoiditis without complications. It was suggested that the author influence the focus therapeutically. He used the antivirus of Besredka. The results were not encouraging; perhaps the unfavorable anatomic conditions of the middle ear were responsible. Good results, however, were achieved by local treatment of otitis externa with staphylococcus vaccine. As a rule, a certain disposition or constitution is necessary for the tympanic cavity to become infected. This also holds for the propagation of the process. It could be observed especially plainly during the epidemic of the grip, when grave complications occurred more frequently, and after measles, scarlet fever, tonsillitis, etc.; it could also be observed in diabetics, in which grave complications were noted. These dispositional and constitutional factors must be taken into consideration when an operation is to be decided on. In the majority of cases, it could not be established that such factors favored the infection, but they might be present. The disposition to a suppuration of the middle ear and its complications may be based on anatomic conditions. The author has considered especially the character of the mucous membrane of the middle ear on which the pneumatization of the mastoid process depends, according to Wittmaack.

Hyperplasia of the mucous membrane facilitates an infection. An extensive destruction is found in a mastoid process with small cells, with an average degree of hyperplasia of the mucous membrane. Perhaps conditions unfavorable for an escape of secretions come into play, owing to the inflammation and swelling of the thick mucous membrane which lines the small cells. Normally pneumatized mastoid processes, the structure of which is based on a normally involuted mucous membrane, were found rarely. Generally an infection of the mucosa was present. The cases in which *B. mucosus* was involved showed that age and sex are, to a certain extent, important in an infection.

An infection of the middle ear depends on many factors. The bacteriology, the virulence, the blood picture, etc., or the roentgenogram showing the character of mucous membrane alone cannot determine the cause of the infection. Neither do they allow a prognosis. All these factors must be considered in their totality. Naturally, there are cases in which a single factor comes to the fore. For instance, extremely virulent microbes may cause an infection under otherwise normal physical conditions. The difficulty of judgment by virtue of all these components consists in the fact that nothing sure is known concerning the relation of disposition and constitution to infections, with the exception of the anatomic constitutional factors mentioned before. There remain unknown factors which must be considered and evaluated by the clinical eye and experience. But also the bacteriologic and roentgenologic observations will give assistance.

EXPERIENCES CONCERNING MUCOSUS OTITIS. KLAUS VOGEL, Ztschr. f. Hals-, Nasen- u. Ohrenh. **22**:357 (Jan. 7) 1929.

In 288 cases in which operations were performed, the following microbes were found:

	No. Times	Per Cent
Streptococcus hemolyticus	147	51.0
Streptococcus, staphylococcus	15	5.2
Streptococcus hemolyticus + influenza bacillus	1	0.3
Nonhemolytic streptococcus	24	8.3
Nonhemolytic streptococcus + staphylococcus	7	2.4
Staphylococcus	23	7.9
Pneumococcus I	4	1.4
Pneumococcus II	1	0.3
Pneumococcus III and Streptococcus mucosus	52	18.2
Pneumococcus IV	2	0.6
Friedlaender's bacillus	3	1.0
Proteus	8	2,7
Bacterium coli	1	0.3

Of the 50 patients with mucosus otitis who were operated on, 30 were men, 10 women and 10 children (4 girls and 6 boys). Two cases had to be omitted because the histories could not be obtained. Of the 40 adults, 25 presented the typical picture of mucosus otitis, showing a progressive course with few symptoms. In 25 cases, complaints had been either not pronounced or totally missing, except disturbances of hearing. In 20 cases, the disease had existed for from six to twelve weeks before the operation, and in one case seven months. The duration of the disease was always surprisingly short in nurslings and infants. In 5 cases, the drum was not perforated, although there was a continuation of the process under the skin. The temperature in children was normal in half the cases. Frequently, postauricular swelling was the first prominent symptom. Of 10 children, 1 died of meningitis and 1 died later of erysipelas. There were many endocranial complications, both single and multiple, in 27 of the 50 patients: extradural abscess alone in 4 patients; perisinuous abscess alone in 7 patients; extradural and perisinuous abscess in 5 patients; meningitis alone in 5 patients; meningitis, sinus thrombosis and cerebellar abscess in 1 patient; meningitis and perisinuous abscess in 2 patients; meningitis and extradural abscess in 2 patients, and meningitis and extradural and perisinuous abscess in 1 patient.

Of the 11 cases of meningitis, 5 followed labyrinthitis. In 9 instances, the fatal meningitis appeared suddenly and unexpectedly. Besides the endocranial complications, 5 cases of Bezold's mastoiditis were observed (once alone, once with extradural abscess and twice with a perisinuous abscess). The mortality rate was 24 per cent, whereas the mortality rate in cases with a mixed bacteriologic etiology, including *Streptococcus mucosus* was 7 per cent. The idea of Stuetz that mucosus otitis preferably attacks the normally pneumatized mastoid process cannot be sustained. In the summer and in the fall, infections with *S. mucosus* were rare. They were more frequent from December to March, and most frequent in January, February and March. In the adult, the course shows few or no characteristics. In a few cases, the characteristic picture of mucosus otitis can be produced by other microbes, the streptococcus, Friedländer's bacillus or the proteus, if the patients are old, if they have a weak reaction or if they suffer from diabetes. *Streptococcus* mucosus is identical with pneumococcus III. The clinical picture frequently furnishes the diagnosis, but not always.

AMBERG, Detroit.

Diseases of the Skin

THE ECZEMA-ASTHMA-PRURIGO-COMPLEX. R. CRANSTON LOW, Brit. J. Dermat. **40**:389 (Oct.) 1928.

Cranston Low discusses this subject in detail with numerous references to the literature. The subject is taken up under the following subheadings: prurigo and eczema; association of eczema and asthma; protein skin tests; heredity; blood changes in asthma; eczema and prurigo; ichthyosis, eczema and asthma; and

alternation of eczema and asthma. He comments on the lack of mention of the association of eczema and asthma in many of the modern textbooks on dermatology and asthma, and feels that the subject should be thoroughly discussed in the light of the modern conception of the two conditions and their association with anaphylaxis and sensitization. In a statistical study he found that in a considerable number of cases of chronic eczema there was a history of asthma and vice versa. The fact that both chronic eczemas and asthma give positive skin reactions to various proteins suggests that in cases of combined asthma and eczema the same protein is responsible for both conditions. The author cites a case in a girl, aged 9 years, with eczema and asthma in which both conditions were dependent on the ingestion of sugar. He states that the experience of those who have used protein skin tests in sensitization diseases is that the younger the patient the more frequently food proteins are responsible, while later in life, animal emanations, dust and bacterial antigens from focal infections play a larger part in the etiology. He comments on the relation to this group of dermatitis venenata or eczema due to an external cause from the contact with the skin of some substance to which the skin is sensitized, and states that the corresponding lesion in the respiratory tract is hay-fever.

He concludes with the statement that asthma-eczema and asthma, from their clinical course, symptoms, hereditary tendencies, skin tests and changes in the blood and other tissues, are analogous in every respect. This being so, the surprising thing is not that eczema and asthma may occur in the same patient, but that they are not more often associated.

[Arch. Dermat. & Syph.]

The Asthma-Eczema-Prurigo Complex. J. A. Drake, Brit. J. Dermat. **40**:407 (Oct.) 1928.

The subject is discussed in a general way, and Drake states that it is not unreasonable to put forth or support the hypothesis that the underlying or basic factor in the asthma-eczema-prurigo complex is an inherent, or possibly acquired, dysfunction or disharmony of the autonomic nervous system.

[Arch. Dermat. & Syph.]

On the Psychic and Nervous Component of the So-Called Allergic Skin-Diseases and Their Treatment. W. T. Sack, Brit. J. Dermat. **40**:442 (Nov.) 1928.

In examining the mental condition of all patients coming to him as a skin specialist, Sack was struck by the numerous connections between diseases of the skin (especially pruriginous ones) and mental and emotional irritation. In many cases he was able to succeed, by hypnotism alone, in causing pruritus, which had previously resisted all kinds of treatment, entirely to disappear. In speaking of allergy, Sack states that allergy imputes a complete change of the whole organism, and though fixed to and manifested in the special organ, it brings the question down to the problem of the whole constitution of the individual. He mentions the fact that recent publications seem to indicate that the similarity of certain allergic skin diseases may not be based on this quality alone but also on a specific alteration of the autonomic nervous system. In some cases the same symptoms as noted in allergic diseases are found and the slightest sign of allergy is not noted as, for instance, in cases in which the symptoms are produced by purely psychic factors. It is further an established fact that a correlation exists between the autonomic nervous system and the endocrines, and that malfunction of one cannot be present without disorderly action of the other. Working on this basis the author has been using in certain cases of eczema and neurodermatitis a synthetic ephedrine, called ephetonin, with favorable results.

[Arch. Dermat. & Syph.]

THE ACTION OF ULTRAVIOLET RAYS ON THE SKIN. ALBERT EIDINOW, Brit. J. Tuberc. **22**:136, 1928.

The present conception of the action of ultraviolet rays on the skin supports the theory of the production of (1) local photobiochemical substances which have bactericidal or vitamin properties; (2) local hyperemia of the skin; (3) stimulation of a leukocytic infiltration of the epidermal tissues.

H. J. CORPER.

TREATMENT OF URTICARIA AND ALLIED DISORDERS WITH CESIUM EOSINATE. H. GOUGEROT, E. PEYRE and F. BERTILLON, Bull. Soc. franç. de dermat. et syph. **35**:530, 1928.

Eosinate of cesium which was found experimentally to possess anti-anaphylactic effects was used by the authors in certain cutaneous allergic diseases with encouraging results. From 10 to 15 cc. of a 10 per cent solution was given intravenously, daily or triweekly.

[ARCH. DERMAT. & SYPH.]

A CASE OF URTICARIA PIGMENTOSA. L. LORTAT-JACOB and T. BROSSE, Bull. Soc. franç. de dermat. et syph. **35**:560, 1928.

A typical case of this disorder in an infant, aged 1½ years, was presented. In discussing this case, Cailliau stated that his histologic investigation led him to regard urticaria pigmentosa as the result of a local hematopoiesis, which allied it with the lymphoblastomas.

[ARCH. DERMAT. & SYPH.]

FAVUS OF THE LID AND SCALP IN AN INFANT SIXTEEN DAYS OLD. J. PAYENNEVILLE and J. MARIE, Bull. Soc. franç. de dermat. et syph. **35**:567, 1928.

A case which was clinically typical and verified by laboratory procedures was reported because it represented the earliest reported instance of favus infection; namely, on the fourth day of life. The history was obtained from the family. The authors did not see the patient until she was 16 days old.

[ARCH. DERMAT. & SYPH.]

Surgery and Orthopedics

CONSERVATIVE METHODS OF DEALING WITH EMPYEMA. CHARLES MCNEIL, Edinburgh M. J. **36**:42 (March) 1929.

For children less than 2 years of age, who have a coincident acute pneumonia, surgical procedures are dangerous. McNeil presented three children, aged 5½, 6 and 7 years, respectfully, in whom the simple method of repeated aspiration of the chest was used for from one to three weeks. Later, he inserted and left between the ribs a cannula with a rubber tube attached. No spontaneous drainage occurred, but once or twice daily the pus was aspirated. Later a tiny rubber drain took the place of the cannula. In addition, he used a lotion of a boric acid solution (eusol) for lavaging the pleural cavity; he also used a 1 per cent solution of iodoform suspended in sterile liquid paraffin. The children all made complete recoveries within a few months.

NEFF, Kansas City.

INFANTICIDE BY THE MOTHER DURING BIRTH. G. SCHMIDT, Arch. f. Kriminol. **83**:260, 1928.

There are records of a projecting arm or even the head being severed by the mother with sharp instruments before the child has completely passed out of the birth passage, also of infanticide by stabbing the presenting intravaginal portions of the infant. The child has also been strangled when only the head was born. This report by Schmidt is another of these rare intrapartum murders. The mother beat the child's head with her bare fists so that the top and right side of the

cranium was extensively fractured, and the child died a few hours after birth. When the physician arrived, the feet were still in the vagina, and the bed was bloody where the child's head lay.

E. R. Le Count.

Inheritance of Blood Groups. K. H. Bauer, Klin. Wchnschr. **7**:1588, 1928.

Bauer presents a theory of blood group inheritance, based on the coupling and the exchange of germinal factors. The term coupling of factors refers to the presence of different factors in the same chromosome. The term exchange of factors refers to the breaking up of this coupling and the separation of factors that have heretofore always been transmitted together. This occurs when there is synapsis of homologous chromosomes, with subsequent separation, in which fragments of one became included in the other. This theory explains the O and AB children of O × AB marriages, which Bernstein's theory totally fails to explain, and which Dungern and Hirschfield's theory would lead one to expect in much greater numbers than they actually appear. In 174 O × AB marriages, with 474 children, the latter were found to be distributed among the blood groups as follows: O, 22; A, 216; B, 204; AB, 28.

[Arch. Path.]

Blood Groups and Paternity. G. Haselhorst, Klin. Wchnschr. **7**:1816, 1928.

The blood groups O, A, B and AB in 1,000 men were, respectively, 41.10, 41.80, 13.10 and 3.00 per cent; in 3,000 women, they were 39.33, 43.70, 12.73 and 4.23 per cent. Among 750 determinations of mother and child, 400 of which included also the father, there were only two exceptions to the inheritance rules of von Dungern and Hirszfeld and none to the general scheme of Bernstein. A plausible explanation was found for one of these exceptions, but not for the other.

E. F. Hirsch.

A Pedologic Advisory Clinic in Warsaw. Helen Boguszewska, Opieka nod Dzieckiem **6**:114 (March and April) 1928.

This clinic is for the purpose of investigating why a child becomes delinquent. The mother and child can come to this clinic where each is questioned and where the cause of the condition is discovered and often corrected. The clinic has attained great popularity.

Institutions for the Care of Children in Woj. Kieleckie. Sofie Bykowski, Opieka nod Dzieckiem **6**:132 (March and April) 1928.

A great number of these benevolent organizations sprang up in the last few years to promote health and guard children. From 1924 to 1926, the cost of these organizations was almost doubled.

Bibliographic Information for Child Welfare Workers. Z. Sikorowska and M. Iwaskiewicz, Opieka nod Dzieckiem **6**:150 (March and April) 1928.

Many libraries have been established in different sections of the country for child welfare workers. Books can be procured on any phase of child care.

The Individual and the Sphere of Work for the Good of Society. H. Podlinska, Opieka nod Dzieckiem **6**:201 (May and June) 1928.

Work with children is noble and inspiring and accomplishes most for the good of society. In order to help children, the work must begin early, particularly during the prenatal period. Help for the infant starts with helping the mother.

Krupinski, Chicago.

Miscellaneous

CALCIUM METABOLISM AS RELATED TO THERAPY. HENRY O. COLOMB, M. J. & Rec. **129**:121 (Feb. 6) 1929.

Calcium is present in all the tissues of the body and is a necessary physiologic salt. It is not readily absorbed from the alimentary tract. It is regulated by vitamin D and the parathyroid internal secretion. Physiologically, it is essential to the coagulation of blood, to the rigidity of repair of the bony structure and to the stability of nervous tissue. It has a marked affinity for nitrogen and nitrogenous products. From a therapeutic point of view it is valuable in such diseases as those characterized by jaundice or those accompanied by intestinal toxemia or ulceration of the gastro-intestinal tract. In rickets and hypoparathyroid and infantile tetany, it is valuable as an adjuvant to other measures.

WILLIAMSON, New Orleans.

MATERNITY AND CHILD WELFARE, WITH SPECIAL REFERENCE TO LEGISLATION. M. I. BALFOUR, The Antiseptic, Madras **26**:388 (April) 1929.

The maternity and child welfare situation in India is much the same as it was in England in the beginning of the century, with the difference that the economic condition of the masses is poorer. In England, in addition to voluntary effort, there have been continued legislation and large annual sums spent by the government. In India the effort has been voluntary; the movement was started by women medical missionaries and the wives of officials and gradually was adopted by local bodies.

SANFORD, Chicago.

THE USE OF NARCOTIC SUBSTANCES IN CHILDHOOD. E. ROMINGER, Der Schmertz **1**:272, 1928.

In discussing the use of anesthetics, narcotics, etc., in childhood, the author calls attention to the fact that the central nervous system of the infant and child is less differentiated than that of the adult, and therefore drugs that paralyze or quiet the higher centers may produce harmful results through their action on the respiratory or vasomotor centers. The actions of the various anesthetics are discussed.

For producing general anesthesia in infants and young children, the author recommends a urethane derivative, feeling that it has no bad effects on the respiration or circulation. It is administered rectally. Unfortunately, it is not always swift and sure in its action, particularly in older children. It may, however, be used successfully in combination with a local anesthetic.

The author concludes by stating that no available anesthetic is completely satisfactory, and that further study should be carried on in the field.

LESLIE, Evanston, Ill.

Society Transactions

CHICAGO PEDIATRIC SOCIETY

Regular Meeting, Feb. 19, 1929

M. L. BLATT, M.D., *President, in the Chair*

ASPIRATION IN EMPYEMA. DR. E. T. MCENERY.

Although empyema was known to the ancients and the importance of drainage was recognized by Hippocrates, there are few surgical conditions that have aroused more discussion during the last fifty years concerning the method of treatment. The present concept of aspiration in empyema is that it is not satisfactory and should be used only as a temporary procedure for the purpose of tiding a patient over the acute pneumonia stage of illness, with the expectation of establishing adequate drainage later if necessary.

A new method of treatment is not being advocated, nor is it being claimed that all patients can be treated by such methods. A series of thirty-seven cases of empyema is reported; the patients were treated at the Children's Memorial Hospital during 1928. These patients were taken consecutively. Thirty-three were treated by aspiration. The other four were operated on for the following reasons: two patients had discharging sinuses; one, the attending man, had requested that surgical treatment be used, and the fourth patient had been treated by aspiration outside the hospital and the needle had broken off in the chest cavity. The method has been to aspirate with a number 15 bore needle, with the patient under local anesthesia. Pneumothorax developed in 50 per cent. Five cases occurred spontaneously before aspiration.

The following organisms were cultured: pneumococcus 29, hemolytic streptococcus 2 and staphylococcus 1. No culture was taken in one case. The average stay in the hospital was from two and one-half to three and one-half months. The mortality rate was 9 per cent; one patient died a week after leaving the hospital against advice. The other patients consisted of an infant, aged 21 months, who died of pneumococcus meningitis, and a boy, aged 6 years, with a bilateral empyema. Frequent roentgenograms were taken during the patient's stay in the hospital and on his return visits to the outpatient department in order to show a graphic record of just what happened to the patient during a year.

Physical observations characteristic of practically all cases have been: no deformity of the chest, excursion equal, resonance not impaired, breath sounds on normal inspiration distant, on forced inspiration practically normal. The children had gained in weight, did not cough and seemed to lead a normal active life.

EMPYEMA. DR. RALPH B. BETTMAN (by invitation).

Pathologic changes in the pleural cavity result in numerous changes in the mechanism of respiration. Empyema is no clinical entity as such. There is as much or more variation between cases of empyema than there is between cases of peritonitis. Just as peritonitis is a secondary condition in the vast majority of cases, so is empyema. The course of the empyema varies according to the type of disease to which it is secondary.

The primary condition of the lung is an important factor in the treatment for empyema. If, as is so often the case in bronchopneumonia, an inflammatory condition of the lung is still present, the empyema contents must be removed with great care lest reexpansion of the diseased lung activates the bronchopneumonia. On the other hand, if the empyema is secondary to lobar pneumonia and the inflammatory condition of the lung has subsided, the reexpansion of the lung will in this case be a desirable rather than an undesirable factor.

Certain types of empyema, especially those due to streptococcus, are more prone to be accompanied by such conditions as abscesses of the lungs, abscesses of the brain, otitis media and osteomyelitis. For this reason, it is especially desirable to sterilize the chest cavity as soon as possible in the hope of preventing dissemination of the organisms. In empyemas due to pneumococcus, complications are not so common. Air in the empyema cavity lowers the resistance of the pleura to infection. Pneumothorax interferes with the lymph drainage of the thorax. Swinging of the mediastinum from side to side is provocative of shock. The mediastinum does not form an actual barrier between the two pleural cavities so far as pressure relationship is concerned. If adhesions are present, the hilum of the lung is secondarily fixed and the two cavities may have different pressure values. An infection in a cavity persists until the cavity becomes obliterated, and obliteration of the cavity occurs as the lung is reexpanded.

Obviously, no one clinical method of treatment for empyema can be used, but each patient must be considered and treated according to the intrinsic conditions.

EMPYEMA IN CHILDHOOD (Atypical Cases). DR. PHILIP ROSENBLUM.

A review of the literature on empyema in children discloses that a considerable amount has been written on the diagnosis of the typical case, but very little is found on the atypical cases.

Empyema occurred twice as frequently last year at the Cook County and Michael Reese hospitals as during the previous year—7 and 3 per cent respectively.

Pneumococcus empyema occurs later, while streptococcus effusions appear early and are large. The roentgen rays are of paramount importance in the diagnosis and localization of empyema. When empyema is associated with a pneumonic condition of the lung in the early stages, the x-ray picture may show no characteristic shape. A normal temperature does not exclude empyema. Small quantities of fluid are often missed because of minimum evidence on physical examination and indefinite outline in the roentgenograms.

Interlobar effusion, which is often postpneumonic, may give rise to a confusing clinical picture. A small interlobar empyema may give no physical evidence and may be found only on roentgen examination. Pleuritic bands may still further complicate the diagnosis. The shadows in interlobar effusions vary according to the position of the patient when fluoroscopy is done. It is probably true that in many cases a condition diagnosed as unresolved pneumonia is a small encapsulated empyema which absorbs spontaneously. In encapsulated empyema, even with repeated aspirations, it is often difficult to locate the pus.

Three cases were reported: One followed pneumonia of the left lung. Interlobar empyema appeared as a massive exudate and finally cured itself by rupturing into the bronchus. Case 2 was an encapsulated empyema. It was impossible to obtain pus after one or two aspirations, but the temperature persisted so that thoracotomy was performed. Case 3 occurred in an infant, who recovered after the aspiration of 20 cc. of thick pneumococcus pus.

DISCUSSION

DR. ALBERT H. MONTGOMERY: I think that we are in agreement on most of the points that have been brought up on the treatment for empyema. Dr. Bettman has lucidly described the anatomy associated with empyema, and most of the points underlying the treatment. I am sure we all agree that no single method is applicable to all cases. Instead of regarding empyema as not a definite pathologic entity, I think we should consider that there are variations in its form, but the main thing is its bacteriology. The cases that were presented, showing a bacteriology in which the pneumococcus is the offending organism, differ widely from those in which the streptococcus, staphylococcus and the anaerobes play the leading part. The pneumococcus is benign in its action, while in the other types the opposite is true.

Dr. McEnery is modest in saying that he presents nothing new. That is true, but he has shown an old method with a new application. He has persisted in his tapping of these cases, and has had the courage to stand by his beliefs. It is known that many patients are cured of empyema and infections elsewhere by simple aspiration of the pus. Dr. Bettman emphasized the accepted fact that the pleura is resistant to infection, and there is no question that many of these cases due to the pneumococcus will clear up under repeated aspiration, as Dr. McEnery has shown. We must remember that two thirds of the patients were under 6 years of age, and he has pointed out that the younger the child, the better is the outlook. The younger the child, the closer is the lung to the wall of the chest, and the easier is it for it to expand. That may explain why the lung comes out and obliterates the cavity more easily than in the older children.

I should not wish you to feel that this is a fairly benign process. If we look back on the things that Dr. Bettman emphasized—the removal of the pus, the restoration of the cavity and the obliteration of the cavity—we shall realize this. It is only when the pus becomes thick and filled with fibrin that we know that we are dealing with a localized cavity instead of a generalized infection in the lung. The mediastinum is fixed and we are on safe grounds in treating it. But if we go on with repeated aspirations, how about obliterating the cavity later? As a rule, these patients do not die of acute empyema. They die of a chronic empyema, or of the complications that are associated with it. The condition will sometimes cure itself, if we wait long enough. It will break through the wall of the chest in some instances, but it is not a good form of treatment to allow a case to go on until adhesions form and a thoracoplasty has to be done to remove them.

I wish to offer a word of warning. Although treatment by aspiration may be used early and given a fair chance, it should not be carried on too long—until nothing but thoracoplasty will cure the patient.

Dr. Joseph Brennemann: Dr. McEnery and I were associated in this work, and there are a few points I might emphasize. When we first reported our progress in these cases nearly a year after the treatment was first begun, we had reached the twenty-ninth case with only one death, and that occurred in a case in which the child had gone home against advice. We naturally became enthusiastic, but gradually realized the limitations of aspirations as a sole procedure. As it is, our mortality rate with aspirations alone is one of the lowest on record with any treatment. I do not believe that the fact that 87 per cent of our cases were due to the pneumococcus was a determining factor in our rather unusual success. The pneumococcus is usually stated to be present in about 75 per cent of cases. A number of patients with streptococcus infections have been reported who recovered by aspiration alone, as all of ours did. The thick fibrin masses that are supposed to be a serious obstacle to aspiration did not bother us much, and we can conclude only that they liquefy after a time or are absorbed. The greatest factor in our results was our persistence.

One of the most interesting observations in our series was a 50 per cent incidence of pyopneumothorax. Contrary to the usual view, this did not add materially to the gravity of the case and in a study of this kind the pneumothorax was peculiarly helpful in showing just how much pus was still present and could be absorbed without further aspiration.

Both Dr. McEnery and I would like to state as emphatically as we can that our purpose in this paper is not to recommend a sole method of treatment. We think that there should be no one method of treatment for empyema regardless of the age of the patient. We were increasingly convinced as this work progressed that not only do the infants, in whom the mortality rate with the open operation is extremely high, do better after aspiration than after operation, but that the younger children do better when aspiration is used than do the older ones. In our series of sixteen patients 3 years old and under we lost only one

child, and that child had an insignificant empyema that was merely a part of a pneumococcus septicemia and meningitis.

We believe that aspiration should be done for a time on all children with empyema; that infants and children up to 3 years of age are best treated by aspiration, or the closed method alone; that children of 5 or 6 years or older, if they do not look promising after several aspirations, should be operated on, and in these cases we should prefer an open operation. In the children between infancy and 5 and 6 years of age, we should persist in using aspiration as long as conditions looked favorable.

There is one other point we think of importance: Empyema is never a surgical emergency, and there is good reason for thinking that it is well to incline toward waiting rather than toward hastening with either aspiration or operation.

Dr. S. L. Koch: I wish to report briefly concerning a group of patients who were operated on in 1926—seventeen of them at the Cook County Hospital and two at Wesley Memorial Hospital. The majority were admitted to the medical ward and aspiration was performed a number of times. Various types of organisms were found. It is of some interest in connection with Dr. McEnery's paper that the patient on whom aspiration was done most often and who was in the hospital the longest period of time before being operated on required the longest time for cure after surgical intervention.

In all of these cases a catheter was inserted between the ribs, and after operation constant negative pressure was maintained with the aid of a suction apparatus. Irrigation with surgical solution of chlorinated soda was used every two hours until the infection was under control.

In the series of nineteen cases there were two patients who were in a critical condition when admitted, and who died within thirty-six hours without being operated on. Two other patients died. One, whose temperature was normal and who was apparently recovering, suddenly developed a pneumothorax two weeks after operation and died a few hours later. The other child was discharged as cured, but six days later was readmitted with a reaccumulation of pus in the old cavity. Treatment was reinstituted but he developed fever, a persistent headache, then coma and died two weeks after readmission. Autopsy showed multiple abscesses of the brain, and the old empyema cavity was entirely obliterated.

In the nineteen cases, then, two patients were not operated on and died within a short time after admission. Two of the seventeen patients operated on died.

Last year I had under my care at Wesley Memorial Hospital a patient, aged 6 months, with a streptococcic empyema who was referred by Dr. G. N. Krost. She was operated on as soon as the diagnosis was made. A catheter was placed between the ribs, suction applied and surgical solution of chlorinated soda used for irrigation. At the end of ten days, the fluid withdrawn after irrigation was thin and mucoid, and on culture was free from bacteria. The catheter was removed, the wound healed promptly, and the patient was discharged after some weeks of observation entirely free from symptoms.

Dr. J. H. Hess: Several interesting points have been mentioned that have covered some of the experience I have had with empyema. The first is the question of repeated aspiration. Important for consideration is the underlying type of pneumonia, whether it is lobar pneumonia or bronchopneumonia and whether the empyema follows an acute contagious disease. Uncontaminated infections with pneumococci offer the best prognosis. Streptococcus infections, however, are no exception. We have recently had such a favorable result in a case of massive hemolytic streptococcus empyema following scarlet fever.

In the treatment of about 200 patients with empyema at Fort Riley during the war, 21.2 per cent of the cases of lobar pneumonia were followed by empyema; 32 per cent of the group were complications following measles pneumonia. The bacteriology was completed in 150 cases, and most of them were due to the streptococcus.

During the early part of the epidemic of measles pneumonia, the patients were transferred to the surgical service as soon as the diagnosis of empyema was made with the result that early operations resulted in a mortality rate of 63.9 per cent. Then a surgeon was assigned to us for the care of these patients, for operation after repeated aspiration, with a resulting mortality rate of 22.2 per cent.

During the influenza epidemic, I was transferred to Fort Benjamin Harrison. Only eighteen of our patients developed empyema, and of those fourteen were cured by aspiration, four required operation after repeated aspiration and all recovered.

Aspiration, to be followed by satisfactory results, calls for careful physical examination in order to localize properly the best point of approach. When indicated, operation must not be delayed too long.

The lesson that my war and hospital experiences have brought home to me is that this serious complication calls for teamwork on the part of internist and surgeon.

DR. RALPH BETTMAN: My paper was on the physiology of empyema. As regards treatment, there are four main methods of operation in empyema: first, by aspiration; second, the closed method of inserting a catheter into an intercostal space by means of a trocar, keeping the catheter at intervals; third, resection of a rib and closing the chest, allowing a tube to remain in place, either attached to a continuous suction apparatus or clamped off. These are all closed methods. The fourth is a method which can be used only in the smallest group of cases; that is, a rib resection with the cavity left open. The disadvantages of such an operation are apparent. If the operation is done in the early stages the ending is fatal because of the two reasons mentioned. There is rarely a death from acute empyema if any one of the closed methods of treatment is used.

It is absolutely impossible to compare one set of statistics with another. A streptococcic infection one year differs from that of the next year.

I have never done an open operation on an infant. In the group of thirty-three cases we had last year, I used the tube and closed method. Six deaths occurred, all with secondary complications, which I think we could not have prevented by any method. In those cases the average length of time in the hospital was forty-seven days. We must recognize every one of the underlying conditions and treat the patient with all of these considerations in mind.

DR. EUGENE T. MCENERY: We were fortunate in that we did not have many complications in our group. There were some mild cases of otitis media, but we did not operate. One child had whooping cough and we felt that he probably helped himself get well by means of the incessant coughing.

As to the time element, we thought that if we could have sent the patients home to suitable conditions they could have gone within a month. One case that I demonstrated cleared up in less than two months, showing how rapidly this occurs. In some instances we kept the children in the hospital for five or six months because we wished to watch them and take repeated pictures, and also because their home environment was not satisfactory.

Regular Meeting, March 19, 1929

M. L. BLATT, M.D., *President, in the Chair*

A CLINICAL STUDY OF MENINGOCOCCUS MENINGITIS. DR. MAXWELL P. BOROVSKY.

In the ward for contagious diseases at the Cook County Hospital, 190 cases of meningococcus meningitis were observed from January, 1927, to September, 1928, and 5 instances of more than one case in a family were noted. Negative Kernig

and Brudzinski signs were recorded in only nine cases, all of these patients being between the ages of 3 and 20 months. Otherwise, headache, vomiting and fever were universal symptoms; rigidity of the neck, however, existed merely as an increased resistance to anterior flexion of the head in young infants. Bulging fontanel was observed in every case in infants whose fontanels were still open. Convulsions were noted in only 6.5 per cent of the cases, all in children, with a mortality rate of 58 per cent. Petechiae occurred in 6.7 per cent; herpes in 10 per cent, and strabismus in 12.5 per cent. Ptosis was observed in only four cases, unequal pupils in three and nystagmus in six. The average stay in the hospital of the patients who recovered was 19.6 days. The mortality rate in this series was 48.9 per cent, being greatest for patients under 1 year and over 50, and lowest in those between 10 and 12 years. Patients entering in a state of coma had a poorer prognosis. Meningococci were found in all but 6.76 per cent of the cases. The average spinal fluid cell count was 11,780; the lowest, 960.

Polyvalent antimeningococcus serum was administered by daily spinal punctures, the average amount of serum injected into the patients who recovered being 162 cc., intrathecally. In eight instances 50 cc. or less effected a cure. Patients who received intravenous serum therapy, in addition to intrathecal, were chosen at random, and the mortality rate in this group of sixty-eight patients was 57.3 per cent. Shock from spinal puncture occurred only in patients in whom intravenous therapy had been used.

Sixty-one patients were reexamined from two to sixteen months after discharge from the hospital, and 55.7 per cent of these had no complaints. Deafness was the outstanding sequel in 25.4 per cent, and two patients developed deafness two and one-half and three months, respectively, after discharge from the hospital. Persistent strabismus was found in only one instance.

INTERPRETATION OF ROENTGENOGRAMS OF THE CHEST IN CHILDREN, BASED ON NECROPSY OBSERVATIONS. DR. JOHN A. BIGLER.

The lungs of 171 children coming to necropsy were studied to determine what pathologic changes were present to account for the shadows found in the roentgenograms of the chest. By making films of the excised lungs, into the bronchi and blood vessels of which had been injected opaque solutions, it was found that the hilar shadows and linear markings were made up for the most part of blood vessels. The rounded shadows of even density occurring along the linear markings and in or near the hilum were due to blood vessels running parallel to the axial ray. Lymph nodes do not cast shadows recognizable as such unless they contain calcium.

Evidence of tuberculosis was not found pathologically as frequently as it was diagnosed from films of the chest. Fewer errors will be made in diagnosis if the pathologic changes of the childhood type of infection are considered. Shadows due to calcification were found to have a characteristic appearance, and they should not be confused with other shadows, especially when more than one film is taken. The pathologic changes and corresponding roentgen shadows of tuberculosis, pneumonia, collapse of the lung, asthma, emphysema, pyopneumothorax, pneumothorax, thymus and mediastinal tumors were also described.

From a roentgenologic standpoint, it is impossible to formulate any standard for a normal chest. Interpretation of the roentgenogram should go hand in hand with the history, clinical and physical observations and the laboratory data.

DISCUSSION

DR. JOSEPH BRENNEMANN: One sees every day the child on whom a diagnosis of tuberculosis has been made and in whom we, with every means at our command, can find no evidence of tuberculosis. A common cause of this erroneous diagnosis is a roentgenologic interpretation of a roentgenogram of the child's chest. We all know the roentgenologist who has a sort of tuberculosis complex, but even in the absence of that it is difficult to see how the roentgenologist can make an accurate

diagnosis without either knowing all about the clinical and physical observations of the child or without having had an extensive postmortem check on his interpretations.

I have been very much interested in the roentgenogram of the chest ever since it was first used and during the last year and a half, since this work of Dr. Bigler's has been carried on, I have learned more than I knew in all the years before and really feel for the first time that when I look at an x-ray picture I have some concrete reason for my interpretation of it. It is what one sees and not what one hears that is remembered.

We have been especially interested in hilum shadows in which density alone means little, but form, location and the like mean everything. Another thing that has impressed us very much has been the frequency with which the roentgenologic "calcified gland" is not a postmortem calcified gland. In our series, calcified glands have been infrequent, and when they do cast a shadow there is no difficulty in differentiating between a true calcified gland and the round or oval variable shadows that are commonly called calcified glands and are commonly due to blood vessels taken endwise.

DR. C. H. WARFIELD: Whenever any one presents a paper in which he discusses the roentgen and pathologic observations together, there is little room for discussion. One of the German workers not long ago published a review of about 10,000 cases of tuberculosis of the hilum, and in his conclusions stated that we do not yet know how to diagnose tuberculosis in children. At Johns Hopkins Hospital the diagnosis for children is made by consultation with the pediatric staff.

I think the time is coming when the term "x-ray man" will be dropped, and the sooner physicians drop the idea of being so self-centered in each branch, the better it will be. The younger physicians are being taught the value of consultation, but some of the older ones are still dogmatic in interpretation. It was interesting to see how Dr. Bigler brought out the facts he has found. I did not know that calcified glands were diagnosed so commonly, for whenever there is a calcified gland in any part of the body there is no difficulty in finding it.

I think that roentgenography in children is difficult on account of the movement of the child and many other problems of technic entering into the work. I have been much interested in lateral films, principally in adults, and have learned much, for in these views one sees the posterior lobe.

We have had a good deal of experience in the diagnosis of lesions of the thymus gland. Roentgenograms should give a lateral view, for if there is any compression of the trachea one is sure to be dealing with an enlarged thymus.

In regard to the normal or negative chest, a group of eminent physicians appointed by the National Association of Tuberculosis found that there were many variations of the adult chest, apparently in the normal limits, and much lasting evidence of previous diseases was found in the clinically normal chest, and it was decided to discontinue the term "normal chest" and adopt that of "healthy chest." I mention this in the hope that in the future we shall adopt this term and all speak in the same language.

DR. BENJAMIN M. GASUL: I feel that I have learned a great deal this evening, and several points came to mind. The results obtained by Dr. Bigler were also obtained by other investigators. Assman was among the first to show that the markings in the hilum were made up mostly by the blood vessels and not by the bronchi. When I was studying tuberculosis with Dr. Wineberger and Dr. Priesel I was rather surprised to see that many areas of hilar involvement that had been interpreted as calcified glands were cross-sections of blood vessels, which was brought out by Dr. Bigler. We studied 404 tuberculous infants at Professor Pirquet's clinic, and at the time when a diagnosis of tuberculous involvement was first made the majority of these cases did not show any positive roentgen observations. In many cases, the diagnosis was based on a history of exposure and the presence of a positive tuberculin reaction. In the majority of cases of tuberculosis of the hilum the Ghon tubercle and the enlargement of the tracheobronchial lymph glands are not large enough to be shown on the x-ray plates. It takes from two

to five or six years before the Ghon tubercle or the hilum glands show up as calcified areas on the x-ray plate. The triangular area from the hilum is known as Sluka's areas and does not necessarily signify a tuberculous involvement.

DR. CASSIE B. ROSE: I wish to call attention to the fact that Dr. W. W. Wasson of Denver has been doing a great deal of x-ray work on the normal chest in children. He publishes much of it in the roentgenologic journals.

NEW YORK ACADEMY OF MEDICINE, SECTION OF PEDIATRICS

March 14, 1929

STAFFORD MCLEAN, M.D., *in the Chair*

THE DETERMINATION OF THE VALUE OF SERUM IN THE TREATMENT OF MENINGOCOCCUS MENINGITIS. DR. IRVING SHERWOOD WRIGHT, DR. ADOLPH GEORGE DE SANCTIS and DR. ADELE E. SHEPLAR.

Serum treatment in meningococcus meningitis is generally acknowledged to be one of the outstanding examples of successful serum therapy. That this cannot be looked on as a settled fact without exception will be demonstrated in the accompanying report of a series of cases of meningococcus meningitis encountered in the infants' wards of the Post-Graduate Hospital during 1928. Previous to Jan. 1, 1928, the use of the standard antimeningococcus serums had been attended with satisfactory results. Beginning, however, with the first patient to be admitted in 1928, the hitherto effective treatment was found to be useless.

After three consecutive deaths, an active investigation was instituted to explain the cause of the mortality. A search was made to obtain an effective serum to combat the organism present in the cases. Seven different standard and widely used serums were tried in the endeavor to determine an effective one. They will be known in this report as serums 1, 2 and 2A, 3, 4, 5, 6 and 7.

Before a curative serum could be found, ten deaths were recorded among the patients treated with five other serums. The use of the only effective serum, known as 2-2A, was followed by thirty recoveries in a series of thirty-four cases. Two of the patients who died were admitted in a moribund condition in a late stage of the disease (one twenty-two days after the onset); the other two died of a complicating pneumonia after serologic examination of the spinal fluid showed marked improvement.

A positive culture was obtained from the spinal fluid in all but one case. Strains from thirty-two cases were isolated during the late winter and spring months of 1928. All were type 1, except one which was type 2. In seeking a satisfactory serum, the agglutination test was used, since it was the most generally accepted laboratory test for the determination of the potency of a serum against a specific organism.

All antimeningococcus serums for general use are supposed to be polyvalent and effectual against all strains of meningococci likely to be encountered in the area of their distribution. The type of meningococcus present in these cases is one for which all polyvalent serums should contain curative substances. Five were decidedly lacking in this respect. Of the serums used, all were prepared with the use of from thirteen to seventeen strains of meningococci divided among the four groups, except 2-2A and 6. These were prepared with the use of only six strains.

The clinical results following the use of serum 2-2A when compared with those following the use of the other serums in this series, seem to indicate that there may be a loss in specificity against a certain strain of meningococcus when a large number of strains have been used in the production of a polyvalent serum.

The agglutination test, although widely accepted as an index to the curative value of a serum, seems entirely inadequate in the light of the present experience. This is not a new observation. All agglutination tests were carried out uniformly and under standard conditions. Serum 3 equaled all other serums in its agglutinative action against the twenty strains used, and in most cases surpassed them. In the three cases in which it was used therapeutically, it was powerless to control the infection. Although serum 2-2A was not universally as high in agglutinin content as some of the other serums, it was very specific and curative in its action in all cases when administered early. No other serum appeared to contain curative properties against these strains.

Against strain 15, serum 2-2A contained a lower agglutinin content than all other serums, but it did not fail in its curative properties.

All patients treated throughout with serums other than serum 2-2A died.

All but four of the patients treated with serum 2-2A alone were cured. Two of these were moribund on admission and two died of pneumonia after the spinal fluid became practically normal.

1. It must be concluded, then, that the agglutination test is not uniform and is unreliable as a guide for determining the value of a serum against a certain strain of meningococcus.

2. As other methods, such as the opsonic index and the complement-fixation test, have not proved of value in this determination, the therapeutic test appears to be the only reliable method of determining the curative value of a serum against a specific organism.

3. This test may result in fatality in the treatment of a patient, yet be invaluable, as in the present experience, in the treatment of a series of patients.

4. When a patient with meningococcus meningitis fails to respond to treatment, one cannot justifiably conclude that the strain of organism encountered is resistant to serum therapy but only that the serum used is not specific for that organism. It is necessary then to seek an effective serum.

THE LACTIC ACID OF THE CEREBROSPINAL FLUID AS A PROGNOSTIC AND THERAPEUTIC GUIDE IN MENINGITIS. T. GARCIA, DR. A. DE SANCTIS and JOHN A. KILLIAN.

An intensive study was made of the sugar and lactic acid of both the blood and the spinal fluid in meningitis and in a wide variety of pathologic conditions. The object of this investigation was to determine whether variations in the lactic acid of spinal fluid in meningitis could be utilized as an index of the progress of the infection or of a response of the patient to therapy. An increase above the normal amount of the lactic acid in the spinal fluid was observed in epilepsy, chorea, convulsions of nephritis and acute infections. In all of these conditions, however, the lactic acid of the blood exceeded the lactic acid of the spinal fluid.

In meningitis, however, the lactic acid of the spinal fluid was markedly increased, from four to six times the normal amount, and exceeded that of the blood. With clinical improvement, the lactic acid of the spinal fluid diminished and approached that of the blood. The persistence of the lactic acid of the spinal fluid at a high level was thought to indicate a failure of response to treatment and a poor prognosis. Variations in the amount of lactic acid in the spinal fluid in meningitis have proved of greater practical value from a prognostic standpoint than variations in sugar.

Glycolysis of the spinal fluid from meningococcus meningitis with high cell content is analogous to the phenomenon of glycolysis in vitro observed in whole blood, in semen and in synovial fluid containing leukocytes. Glycolysis was not observed in the spinal fluid from normal persons.

DISCUSSION

DR. ROGER H. DENNETT: You may wonder why in this series of forty-four cases we should have continued the use of a serum which was obviously worth-

less. The reason was that we were unable to obtain the serum that we knew to be potent. You may imagine our hopeless attitude when we found patients dying with meningitis when we believed them to be amenable to treatment with any form of serum. We might just as well have been giving so much water intraspinally as the serum that we had at hand. Of course, in the first few cases we did not realize that it was the fault of the serum, but as time went on, it was obviously the reason for our failure to cure. When we discovered that only one of the serums was of any use we had a great deal of difficulty in obtaining this serum. This points to the fact that we must in some way or other keep up our interest in the potency of serums of this sort. We know that the strains of meningitis and other diseases change from year to year. It would seem, therefore, that our laboratory workers should have their interest aroused to the question of keeping the serums potent.

The rest of Dr. Wright's paper was obvious. The agglutination test early proved useless; other tests have shown the same fact. How can help be obtained in individual cases? Dr. Wright has pointed out that we only discovered this in our series of cases, and that perhaps the serum we used in 1928, although it still seems to be potent, may not be potent in the future. This was an interesting observation.

I personally saw most of these patients. We were greatly disturbed at the time about the results we were getting, but did the best we could under the circumstances. When we found that the serum that was potent could not be obtained in sufficient quantity, we then tried other serums, none of which was potent in these cases. We did not try them extensively, but tried them in one or two cases and found that the children died in spite of treatment.

The serum that proved to be potent was the serum that we obtained from the New York State Laboratories.

DR. AUGUSTUS B. WADSWORTH: Although I have been especially interested in the problems relating to the preparation and standardization of antimeningococcus serum for the treatment in meningococcus meningitis, the progress that we have made in the last ten years is largely, if not entirely, due to the work of Miss Kirkbride who has charge of the laboratories engaged in the production of serums and vaccines.

The difficulty of determining therapeutic potency by laboratory tests has been generally recognized, as appears in the report of the International Conference in Paris in 1922, when I served as chairman of the subcommittee that considered these problems. There is no satisfactory laboratory test determining the action of an antitoxic nature because the toxic products of the meningococcus in culture cannot be satisfactorily standardized. The protection test, notably that which Gordon has suggested, has proved unreliable. Similarly, the titration by complement fixation, the opsonic test and bacteriotropic determinations have been advocated by various observers, but have not been accepted. The agglutination test remains as the only practical measure of the extent of the immune reaction and of its polyvalency that can be accurately determined, but this test has never been universally accepted as a reliable indication of therapeutic potency; hence our interest in and dependence on the comparison of the results of laboratory standardization with those of serum therapy of the disease under the most favorable conditions. We have been fortunate in securing, from a number of the larger important medical centers, reliable data from time to time to make these comparisons. Through these reports, our clinical contacts have been greatly extended, not only in this country, but abroad.

Thus, this clinical control of the action of the serum in the treatment of the disease has obviously been essential to the progress which has been made in the last ten years.

The development of serum therapy in meningococcus meningitis is due largely to Flexner's convincing studies in a large number of cases, although reports on a limited series of cases had already appeared in the literature. The earlier methods of the production of serum were directed to the development of a satis-

factory polyvalent serum, especially since several groups of the meningococci were recognized and the classification of the species was not clearly established. The fact that meningococci were isolated from the fatal cases in which there was no response to serum treatment, together with the fact that many of these meningococci failed to agglutinate in the polyvalent serum, led to the addition of these strains as antigens in the preparation of the serum. At the time that we undertook the preparation of serum in Albany, sixty strains of meningococci were used in the preparation. We also encountered nonagglutinable strains, but in some instances these occurred in cases in which there was response to treatment, and further studies of the strains which failed to agglutinate when recently isolated revealed the fact that after cultivation they either agglutinated or could be classified by their antigenic action into the well known types of meningococci. As a result of these studies, the number of strains in the laboratory accumulated so that we had a representative collection.

At this time, Dr. Gilbert made a study of all these strains to select those which proved most typical and most active antigenically in the immunization of animals. It was thought that in these earlier methods of preparing the serum, too much attention might have been paid to polyvalency and that an unnecessary or excessive number of strains were used as antigens in the immunization of the horse, especially as the serum of a horse under immunization with a single strain loses some of its specific action and becomes to some extent polyvalent. The progress which we have made depends on these studies to determine the effect of immunizing horses with different representative strains, limiting the number; it was only after the clear demonstration of the increase in both the agglutination potency and the polyvalency, as determined by tests on a large number of strains of all groups, that this new type of serum was distributed for clinical use. The results of these studies were presented at the meeting of the Laboratory Section of the American Public Health Association in 1919, and published in the *Journal of Experimental Medicine* in January, 1921.

Graphic records of the laboratory tests strikingly illustrate the fact that the six-strain serum possesses not only a greater potency for the homologous strains and all cultures of the recognized groups, together with the atypical unclassified or irregular strains, than any of the other serums, but it is also quite stable — retaining its potency for at least two years. The clinical reports of its use have been without exception most reassuring — confirming the significance of the laboratory study. Nevertheless, statistics of the mortality of the patients treated, when considered collectively, are not nearly so striking, but these patients include a large number treated under unfavorable conditions. Although cases in which the patients were known to be moribund when first treated were eliminated, it was not possible to make this list complete.

For example, the mortality in 144 cases reported since our last publication was 25 per cent. In the cases reported to have meningococci in the spinal fluid the mortality was 38 per cent for patients less than 1 year of age; 14 per cent for patients between the ages of 1 and 10 years, and 37 per cent for 27 patients more than 10 years of age. The list of deaths from which these mortalities were computed include a number that should possibly be eliminated. One patient was treated on the fifteenth day and died on the seventeenth; another was treated on the fourteenth day and died on the sixteenth, another on the twenty-second day and died on the twenty-eighth. Two patients died of bronchopneumonia and two of lobar pneumonia. Two patients less than 1 year of age died of block. The spinal fluid was reported to have cleared in some of these complicated cases in which patients died of other conditions. Thus, we have been forced to rely chiefly on the best equipped hospitals for the most reliable clinical data concerning the action of the serum — clinical reports on a limited series of cases in which treatment was given under the most favorable conditions, such as I have already mentioned.

The importance of standardization and governmental control must be obvious to every one, although extremely difficult on account of the care that is necessary to maintain the highest standards of potency and polyvalency. It is largely on

this account that independent standards for the sale of antimeningococcus serums in the state of New York were established by the Public Health Council in the Sanitary Code of this state, and the Albany laboratory has distributed standard strains of meningococci and serum representing the minimum standard of potency for distribution. The serum offered for sale in the state of New York must also be labeled as to its potency as determined by the agglutination test with these standard strains in comparison with the control serum. It was found necessary to safeguard the interests of the state by the establishment of these standards. They, however, do not apply to the Greater City of New York since the Public Health Council has jurisdiction only over the state, exclusive of the Greater City of New York.

Interest in the improvement of antistreptococcus, antipneumococcus and antimeningococcus serums has recently led to many attempts to concentrate these serums by methods similar to those which are used in purifying or concentrating diphtheria and tetanus antitoxins. Hitherto these attempts have not been altogether successful. The concentrated product has shown a greater potency than the original serum, but the concentrated products which we have studied in the past have not exceeded the potency of the untreated serums of the highest potency attainable. The loss has been considerable, and the gain not in proportion. Moreover, the stability of the concentrated product and the effect of chemical treatment, namely, changes in the protein on the therapeutic potency, have not been fully determined. Our studies are limited to only a few of these products, but I have noted with some concern the published reports of the use of concentrated antimeningococcus serum, knowing the difficulties of determining the therapeutic potency of these serums. There should be a clear demonstration, at least by the laboratory test, of increased potency. Our position is most difficult. We should not rely on the laboratory test of the serum; on the other hand, it is extremely difficult to secure satisfactory comparative clinical data concerning the action of different serums.

THE PATHOLOGY OF SO-CALLED ACUTE PYELITIS IN INFANTS. DR. JAMES R. WILSON and DR. OSCAR M. SCHLOSS.

Fever and the presence of moderate or large amounts of pus in the urine of infants or young children usually lead to the diagnosis of pyelitis. Based on these criteria, pyelitis is a common disease, but the frequency with which it is diagnosed clinically is in striking contrast to its extreme rarity at postmortem examination. For this reason a number of observers have been led to doubt the dependence of pyuria in the young on inflammation of the pelvis of the kidney and suggest its origin in some other part of the urinary tract (Thiemich, Bugbee, Chown and others).

During the past twelve years we have had an opportunity to study the postmortem material on forty-nine infants whose urine contained pus during life. A study of this material demonstrates, we believe, that the usual cause of so-called acute pyelitis in infants is a true suppurative lesion in the interstitial tissue of the kidney.

In the earliest and simplest form, these lesions are small interstitial foci of small mononucleated and polymorphonuclear cells, frequently adjacent to small blood vessels. As the disease advances or is more severe, the lesions are of larger size and contain more polymorphonuclear cells. In the severest form, the picture is that of acute suppurative nephritis and frequently presents frank formation of abscesses.

The early or milder cases produce only slight destruction of adjacent kidney tissue and probably heal without the formation of scars. More advanced lesions lead to varying degrees of necrosis and in healing are replaced by fibrous tissue.

In no case have we observed pyelitis as an isolated entity. Two of our cases disclosed inflammation of the kidney pelvis, but in these, inflammation of the interstitial tissue of the kidney was present and of more marked degree.

PERSISTENT PYURIA IN INFANTS AND CHILDREN. DR. JOHN D. LYTTLE, DR. MEREDITH F. CAMPBELL and DR. PEARL SUMMERFELDT.

In the past two years, we have had under observation in the Pediatric Division of Bellevue Hospital 145 cases of pyuria. Of these, 70 cases have been classified as acute, 17 as recurrent and 47 as persistent. In the last group 30 patients have been given complete urologic examination or have come to necropsy.

Patients with recurrent and persistent pyuria are the most interesting and the most difficult to treat. By recurrent or relapsing pyuria I mean repeated attacks of pyuria accompanied by infections of the upper respiratory tract or other regions; by persistent pyuria, gross or microscopic pyuria for from six weeks to ten years or longer. It is difficult to differentiate between these two types, but usually the recurrent pyuria will clear up entirely in the interval, whereas the persistent pyuria will show gross or microscopic pus whenever an examination is made. There are some cases which, from the history, physical observations and urinalysis alone, cannot be differentiated. The pathology and the prognosis are different in each type of condition. In recurrent pyuria there are repeated attacks of interstitial purulent nephritis, such as Dr. Wilson has described. These acute attacks with fever and pyuria last for a few days and are always accompanied by infections of the upper respiratory tract or other regions. If the patients are examined in the interval, no signs of urinary infection are found. Braasch and Cathcart at the Mayo Clinic note this as a chronic type of urinary infection in adults. They say that after the removal of all foci and after the development of a natural immunity, the patient recovers. In our experience, the last-mentioned factor is the most important in recovery. Many workers report cures of chronic pyuria with various urinary antiseptics. I think they are dealing with a type of relapsing pyuria which tends to clear spontaneously, and not with a persistent pyuria due to obstruction. There is no drug that has any effect in this type of pyuria. As I said, it may be impossible to differentiate these two types clinically, but the most important point is that pyuria in greater or less degree is constant in cases of obstruction.

Most of the children were undernourished and had a history of frequent infection of the upper respiratory tract. The age incidence was from three weeks to twelve years. One third of the patients had had an acute infection recently. In only 16 per cent of cases was there a history of symptoms referable to the urinary tract over an indefinite period of time.

Lumbar pain, renal colic and other symptoms of involvement of the urinary tract are difficult to elicit and evaluate in infants and children. Pyuria is the one symptom that can be relied on for diagnosis. Seven of the patients had an acute onset with urinary symptoms but had no past history referable to the urinary tract. Eight of the patients had a history of an involvement of the urinary tract, as enuresis, urgency, unexplained fever and intermittent abdominal pain. In fifteen cases, pyuria was found on routine urinalysis in children admitted for various other conditions.

In ten cases of recurrent pyuria in which a complete urologic investigation was made, we found no pathologic condition of the urinary tract in any of them. In all of the thirty cases of persistent pyuria in which complete urologic investigation or necropsy was performed, we found a pathologic condition.

I have mentioned nothing new. It is generally known that obstruction and anomaly lead to urinary stasis, infection and destruction of the kidney. Hyman and Beer, Lowsley, Bugbee and Wollstein, Abt, Mixter, Kretschmer, Helmholz and numerous other authors have pointed out the necessity for a complete urologic investigation in those cases of pyuria in which the condition does not clear up with treatment. It seems strange that the point needs emphasis and yet it seems evident that it does. Before we became interested in these cases, two or three cystoscopies were performed a year in the Pediatric Service at the Bellevue Hospital; now we are doing from eight to ten a week with positive observations in 90 per cent, and half of our patients come to us for some other condition. I think the reason is that most of these children have good kidney function. It is easy enough to pick out the patients with hematuria, abdominal tumor, disturbed

micturition, abdominal pain and colic. Very few of these young patients are admitted with these symptoms. In doing this work and studying cases of nephritis, I am more and more struck by the absence of symptoms in the history even when there is extensive damage to the kidneys.

Most necropsy records show a 2 per cent incidence of anomaly of the urinary tract. Bugbee and Wollstein, in 4,903 necropsies of infants, found involvement in 2.3 per cent of cases. Clark, Lowsley and Kingery, in 4,215 necropsies mostly in adults, found an incidence of 1.47 per cent. In 2,420 necropsies of children at Bellevue Hospital we found almost 2 per cent. So, in general, one child in fifty may be expected to have something wrong with his urinary tract. How much trouble this leads to in later life can only be estimated. Kretschmer and others report that from 20 to 30 per cent of urinary disturbances are due to congenital causes. In going over about 12,000 autopsies at Bellevue Hospital, it was found that anomalies of the urinary tract were often the direct cause of death in the first two years; if the patients survived the first two years, the chance of life was good. In 90 per cent of the adults with anomaly of the urinary tract, the cause of death was extrarenal.

Two of the patients, both aged 8 years, with chronic hypertensive nephritis, had changes in the eyegrounds, retention of nitrogen and other evidences of arteriosclerosis. Braasch, at the Mayo Clinic, said that in chronic pyelonephritis when insufficiency of the kidneys develops, the picture is that of interstitial nephritis. Haslinger says that the contracted kidney that develops in the course of a chronic renal infection is different in its etiology and pathology from the ordinary contracted kidney. It may be that these two patients are examples of this kind of secondary contracted kidney. I cannot say that the pathologic condition in the urinary tract of these two patients was the cause of the nephritis and the arteriosclerosis. I think that it may have been. I do not want to be quoted as saying that every child with chronic nephritis should have a cystoscopic examination, but I do think that it should be the procedure for every child with chronic nephritis and persistent pyuria.

DISCUSSION

DR. LINNAEUS E. LA FETRA: These two papers on the subject of pyuria mark an important epoch in the change of ideas on the subject of acute and chronic pyelitis. I presume that physicians have been bound by the old idea that pus in the urine was due to mild inflammation of the pelvis of the kidney, because these patients recovered and were not seen at autopsy. These studies, however, show that there is something else to consider. The work that has been done at Bellevue by Dr. Lyttle and his associates seems important. It takes up the cases which have been troublesome for years, namely, those of persistent pyuria. The least that I can say is that the work shows the importance of a careful study of the whole urinary tract, such as that made by Dr. Lyttle, in all cases in which pus in the urine persists for a long time.

DR. EDWIN BEER: The last two papers on pyuria are comprehensive and cover the subject completely.

The clinical picture known as pyelitis is really, according to pathologic and cystoscopic studies, a pyuria which involves the bladder alone, the bladder and ureter, the bladder, ureter and pelvis, or the bladder, ureter, pelvis and kidney. In the most severe forms, a real pyelonephritis is present.

In all cases of pyuria with a fever that are diagnosed as pyelitis cystitis is present. The most severely sick patients also have pyelonephritis.

The type of infection in these cases is almost invariably bacillary. It seems wrong to call the condition in the kidney suppurative nephritis when the pathologic process is that of pyelonephritis. True suppurative nephritis is rare in bacillary infections, whereas it is common in coccic infections. More than twenty years ago I called attention to the fact that it was difficult to recognize pyelonephritis in which extensive involvement of the kidneys was shown by any functional tests. In these severely diseased kidneys it was accidently noted that the methylene blue (methylthionine chloride, U. S. P.) or indigocarmine (sodium indigotindisul-

phonate, U. S. P.) was deposited in miliary abscesses, and that as they were discharged, the pus appeared in the urine in fair amounts, as was shown by collecting a specimen at every urination; on standing, the pus gradually changed to a blue colorization and the supernatant urine took up the methylene blue, or indigo-carmine, which had been bound to the pus cells in their leukoforms. This late excretion of these two dyes, its reappearance after the primary excretion has stopped, that is, after ninety-six hours, is usually significant of more or less extensive parenchymal involvement in miliary suppurative foci. In a great many cases the observation has been repeated, and in experimental work it has been reproduced. In one case the methylene blue was recovered two and three-fourths years after the last administration.

Cystoscopically, one can confirm the evidence at autopsy as one regularly sees the evidence of cystitis, and in catheterizing the ureters, one may get purulent specimens from the lower level and perfectly clear ones from a higher level, demonstrating that the process is limited to the bladder and perhaps the lower ureter and does not involve the kidney and its pelvis.

All these patients with so-called pyelitis, pyelonephritis or febrile pyurias, should be treated with forced fluids and antiseptics rather than by instrumentation. About twenty years ago there was quite a furore concerning the lavage of these kidneys in adults. Experience has shown that if the infection has involved the parenchyma of the kidney, which may occur more often in adults than in children, such superficial lavages are of no avail, and as a result, repeated lavages have been given up, even though diagnostic catheterization and a single lavage is frequently performed, incidental to the diagnostic procedure. I was surprised that Kretschmer and Helmholz have tried again to reintroduce this questionable procedure of repeated lavage in the treatment of pyelitis in children. I feel sure that it is out of place in view of all the data gathered. I am in sympathy with the more recent view of Helmholz, that patients with these acute conditions should be treated expectantly and with antiseptics. On the other hand, all cases of pyuria that persist for weeks and resist antiseptic treatment with acidification of the urine or alkalinization, or alternation of the two procedures should be examined urologically, as many of the conditions may be explained and properly treated if a careful urologic study is made.

In many cases, despite the most careful roentgenographic and cystoscopic work, the urologist will not be of as much assistance as one would like. Mechanical causes often underlie the persistence of pyuria, and the pictures just shown by Dr. Lyttle illustrate very well the great variety of pathologic disturbances that may lead to persistent pyuria when infection has once set in. The proper way to study these cases is to take a roentgenogram of the genito-urinary tract which may show the presence or absence of calculi which keep up the infection. The x-rays, moreover, may show the size of the kidney or kidneys, if the outlines are clear, and may also demonstrate a hypertrophied bladder filling the pelvic cavity. Palpation may also disclose enlargement of the kidney or the presence of a mass in the hypogastrium after the patient has voided, as so often happens from obstruction to the outflow of urine and a pathologic condition at the neck of the bladder or in the urethra.

Cystograms and cystoscopies will make the diagnosis of these vesical conditions absolute. Many cases, as a result of the cystitis, develop a more or less permanent disturbance in the intramural part of the ureter, which leads to the previously described pictures of bilateral ureteral dilatation, which may extend all the way up the kidney and produce a hydronephrosis. This is probably much more common than is generally realized, and when adults are found with bilateral hydro-ureteronephrosis without obstruction at the neck of the bladder, their condition is probably to be traced to a cystopyelitis of infancy or childhood. If, however, the process is unilateral, it is conceivable that it has been caused by a temporary blockade of the lower end of the ureter by a calculus which subsequently has passed and left in its wake a more or less permanent dilation of the ureter and kidney pelvis. If these ureters are distended and infected long enough, they will probably never return to normal.

In addition to such obstruction, diverticula and narrowing of the lower end of the ureter, there are a great many other conditions, more or less mechanical, which affect the upper urinary tract and may lead to persistent pyuria. Ureteropelvic congenital narrowings, which lead to early hydronephroses, can only be recognized by cystoscopy and pyelography. Many of these cases are observed from childhood to adult life before the unilateral persistent pyuria is explained. By that time the kidney is often useless. Even a most careful operation cannot bring back to normal function a kidney which has undergone chronic obstruction and infection for many years.

In the past, when the process was bilateral, as the pediatrician failed to avail himself of the urologist, the patients usually received treatment for years for pyelitis when they had some of the aforementioned pathologic conditions; they gradually passed into a uremic condition and died. On the other hand, when the process was unilateral, the pediatrician also failed to call in the urologist. These patients frequently became adults; then the urologist was called on to cure a patient with a unilateral source of pyuria.

For more than twenty years I have been trying to interest the pediatrician in a more rational method of treatment for these persistent cases of pyuria. I am glad to be able to express my views before this Section.

PHILADELPHIA PEDIATRIC SOCIETY

JOHN D. DONNELLY, M.D., *Reporter*

March 12, 1929

RALPH M. TYSON, M.D., *President*

THE INCIDENCE OF CONGENITAL SYPHILIS AMONG DEPENDENT CHILDREN. DR. HORACE H. JENKS and DR. JOHN D. DONNELLY.

After carefully reviewing the histories and records of 1,000 children under the care of the Associated Medical Clinic, it was found that 791 were white and 208 were colored; there was one whose color was uncertain. All these children were dependent; that is, there had been some catastrophe in the family which necessitated care of these children by some agency for child care or protection. Their ages varied from 4 months to 16 years. Complete social analyses of the situation in the family were available to the physicians in the clinic, and there was unusual cooperation between the medical staff and social workers from the children's agencies. The physical examinations, which were thorough, were made by the permanent staff of the clinic. Practically all of the Wassermann tests were made by the same pathologist at the same laboratory, using the same technic.

Of the 1,000 children studied, the Wassermann reaction of the blood was definitely positive in twenty-three or 2.3 per cent. Three of these children had lesions of acquired syphilis, so that the incidence of congenital syphilis was 2 per cent. The percentage of positive Wassermann reactions was four times greater for the colored than for the white group. The percentage of illegitimacy among a group of 200 dependent children between the ages of 4 months and 5 years disclosed the unusually high figure of 52.5 per cent. Among this group, however, there was no positive Wassermann reaction. Of the 1,000 children studied, 17.3 per cent were illegitimate, but only one of these illegitimate children had a positive Wassermann reaction. As the physical signs of congenital syphilis are often obscure, it would seem advisable, at least in a clinic for dependent children, to have a Wassermann test of the blood made on every child.

POOLED ADULT BLOOD SERUM AS A PROPHYLACTIC MEASURE IN MEASLES. DR. ALVIN E. SIEGEL and DR. HORTENSE ERMANN.

Measles is so common a disease and frequently so mild an infection that the laity, and even doctors and nurses, fail to show the proper respect for its dangers. The mild manifestations that frequently are shown lead to a reprehensible laxity in the prevention of the spread of the disease. It constitutes a grave illness in all children under 1 year of age; while in its complications, it threatens the health and even the life of older children. In delicate and pretubercular children, it often acts as an activating process for the various forms of tuberculosis. Despite the almost universal susceptibility to the disease, prophylaxis against it is worth the effort, since if it succeeds only in delaying the time of the onset, many lives will be saved.

The specific infecting agent has not been convincingly demonstrated. Various serums have been collected experimentally but have given indifferent results. The blood (whole and serum) of convalescent patients contains specific antibodies, since its injection has given uniformly good results, either entirely preventing the disease or producing an aborted or attenuated form which has, nevertheless, produced a lasting immunity. As the amounts of convalescent serum are limited and as the disease spreads so rapidly and its control is difficult by reason of many unsuspected contacts, some more practical means of prevention should be tried. Since one attack of measles usually gives immunity for life, the serum of adults who have had the disease presumably contains the antibodies. Accordingly, the injection of adult serum should prevent the spread of measles, particularly in an institution for children who are confined and yet exposed to contacts.

During March and April, 1928, an epidemic of measles occurred in the Southern Home for Destitute Children. This outbreak was coincident with an epidemic of the disease among school children of the Philadelphia area. The source of the outbreak in the Home was apparent, as all the children of school age attended the public school. There were 100 children in the home. Between March 24 and April 11, ten children developed typical measles. Thirty-five children gave definite histories of having had measles previously. There remained fifty-five susceptible children. In response to a call for volunteers among the parents of these children, a sufficient number gave blood for the needed serum. Each donor accepted had had measles, was free from constitutional and infectious diseases and gave a negative Wassermann reaction of the blood. The blood was pooled and the serum removed and kept sterile in small vials. The fifty-five susceptible children were inoculated intramuscularly in the region of the buttocks with 5 cc. of the pooled serums on April 15. No untoward reactions followed nor did any fresh cases of measles develop.

Had the end of a self-limited epidemic been reached? Had the epidemic been limited by isolation and hygienic management? Was the absence of new cases due to the definite protection of the serum? The epidemic in the city was still going on and the apparently well children in the Home were going daily to the public schools. Although the cases of measles were isolated as soon as a definite diagnosis was possible, there were still contacts within the Home between susceptible children and the early cases of measles with catarrhal symptoms. It therefore seems reasonable to conclude that prophylaxis by the injection of adult serum was effective.

APLASTIC ANEMIA; REPORT OF CASE. DR. H. BROOKER, DR. MILLS, DR. MICHAEL G. WOHL and DR. SAMUEL GOLDBERG.

B. B., age 7½ years, was admitted to the service of Dr. Mills with the following history: Two months previous to admission, the child had an infection of an index finger and since then had begun to lose color. The change in color became constantly more noticeable. Bed-wetting began one month previous to admission.

The patient's birth was normal; he was breast fed, had a good appetite always, and an occasional pain in the abdomen, followed by headache and vomiting, due

to overeating. There was no history of sore throats; the tonsils and adenoids had been removed because of obstruction to breathing. The patient had mumps three years before, bronchopneumonia two years before, followed by erysipelas of the face and, later, measles.

On examination, the patient showed a pasty-yellow pallor with some puffiness of the face, extremely pale conjunctiva and crusting of blood in the left nostril; the mouth and teeth were in poor condition and the mucous membranes were extremely pale. There was no adenopathy, the lungs were normal and the heart showed a mitral regurgitation, probably of rheumatic origin, but no other changes. There were numerous areas of petechial ecchymoses all over the body. The blood pressure was 60 diastolic, 115 systolic. The urine was normal; the Wassermann reaction, negative. Achromia, poikilocytosis and slight basophilia were present. No platelet cells were found except on November 15 when 8,000 were noted. The coagulation time was three minutes and the retractility of clot, eight minutes. The blood culture gave negative results except on one occasion when *Staphylococcus albus* was found. Blood chemistry studies were all within normal limits. X-ray studies, two weeks after admission, showed a normal chest, but the liver and spleen were markedly enlarged. For one week after admission there was a daily fluctuation of 1 degree of temperature above normal; the pulse rate and respiration were normal. With the onset of pneumonia, the temperature rose to 104 and remained up, ranging from 100 to 104 until dissolution.

Studies of the Blood on Admission in a Patient with Aplastic Anemia *

Cells	On Admission	October 20	October 23	October 30	November 15
Hemoglobin	23	18	12	10	10
Red blood cells	1,120,000	1,010,000	870,000	710,000	510,000
White blood cells	2,650	4,850	4,800	2,100	1,550
Polymorphonuclears	50	30	20	18	14
Small lymphocytes	40	58	63	68	72
Large lymphocytes	8	8	15	8	11
Transitionals	2	1	..	4	1

* The stools were negative for ova and parasites.

Treatment consisted in: care of the mouth and teeth; 2 grains (0.13 Gm.) sodium cacodylate given intramuscularly, at first daily, then every other day; an iron preparation three times daily; seven blood transfusions, about 150 cc. each; daily exposure to quartz light; 0.3 Gm. arsphenamine intravenously (on one occasion); roentgen therapy for the spleen and long bones; red bone marrow in large amounts; broiled chicken livers and liver extracts; dilute hydrochloric acid, 10 minims (0.6 Gm.) every four hours in milk, and brandy for stimulation. For the bronchopneumonia, sodium citrate, aromatic spirits of ammonia and atropine were given.

Intrapleural Injections of Optochine (Ethyl Hydrocuprein Hydrochloride) for Pneumococcic Empyema. Dr. Harry Lowenburg.

This paper refers to nine cases of pneumococcic empyema. All the patients received intrapleural injections of optochine salt (ethyl hydrocuprein hydrochloride). In four of the cases, rib resection and drainage were performed after from four to six injections of optochine. All recovered completely after operation. In five cases, the patients did not come to operation but made complete nonoperative recoveries. The mortality in the nine cases was nil. As much pus as possible was withdrawn before each injection. Then from 5 to 10 cc. of a 5 per cent sterile, watery, warm solution of optochine salt was slowly injected intrapleurally. For the aspiration and injection, Dr. Lowenburg used his own specially devised needle. No ill effects from the optochine itself were experienced. From three to ten injections were made, according to the condition of the patient. The procedure was repeated about every third day.

There was 55.5 per cent of recoveries in patients who received no treatment other than aspiration and intrapleural injections of optochine, one of whom was an infant 4 weeks old. The number and viability of the pneumococci diminished in all the cases in which this agent was used; there was also a retrogressive change in the character of the exudate, even in those which eventually came to surgery, from a thick yellowish pus to a thin serofibrinous and watery fluid. An advantage of this treatment, even though it may have no specific value, is that it delays radical operative procedures, permits a subsidence of the pneumonic and pleural pathologic conditions and makes it possible to increase the patient's resistance, his feeling of well being and even his weight. In the author's cases the patients that came to the operating table had little if any elevation of temperature and were free from dyspnea. All made a speedy recovery. The indications for operation were a reaccumulation of fluid and the persistence of physical signs. Though it is impossible to evaluate completely this method of treatment at the present time, the author states his belief that all patients with pneumococcic empyema should receive it on the chance that they may escape operation; failing this, their chances for recovery are greatly enhanced.

Book Reviews

THE BIOCHEMISTRY OF THE AMINO ACIDS. By H. H. MITCHELL and T. S. HAMILTON. American Chemical Society Monograph Series. Price, $9.50. Pp. 619. New York: The Chemical Catalog Company, 1929.

This excellent monograph deals thoroughly with the whole subject of protein metabolism and includes considerable discussion of metabolism of other foodstuffs. Amino acids, the building stones of the protein molecule, are considered individually and from the standpoints of chemical composition, physical and chemical properties and physiologic action. Qualitative methods for the detection of the individual amino acids and quantitative methods for their determination are given in detail. The metabolism of each of the amino acids under normal and pathologic conditions is considered. This leads to a discussion of such metabolic disturbances as cystinuria, alkaptonuria and parathyroid tetany. The rôle of the amino acids in the production of ammonia for maintenance of body neutrality and for the synthesis of epinephrine, thyroxin, creatine, creatinine and uric acid is fully considered.

The discussion of the composition of protein and of protein digestion, absorption and intermediary metabolism is thorough. Tables giving the digestibility and nutritive value of individual proteins are included. There is a critical discussion of the protein need of the human body and of the possible harmful effect of diets excessively high or extremely low in protein content. The much mooted question of intestinal toxemia receives critical consideration. The book is thoroughly up to date and includes a remarkably complete bibliography. The book is not written in encyclopedic style but is in easily readable form. Each topic is considered in an eminently sound and critical manner, and the experimental work quoted is carefully evaluated. Frequent summations and recapitulations aid the reader in obtaining a clear point of view concerning subjects many of which are not ordinarily easy of comprehension. The pediatrician or any other person interested in the subject of foods and metabolism will find much of value in this monograph.

THE FUEL OF LIFE. By JOHN JAMES RICKARD MACLEOD. Price, $2.50. Pp. 147. Princeton, N. J.: Princeton University Press, 1928.

This book is a careful account of certain experimental work which has been done at Toronto, with an interpretation of the results. It is an excellent and clear exposition, simply written. The main thesis is that fat may be converted into carbohydrate in the internal metabolism. This is in direct opposition to Lusk's contention that such a conversion never occurs. The evidence given indicates that the foundations of the Lusk doctrine are not secure, and, further, it is strongly suggestive, though perhaps largely circumstantial, that this doctrine is incorrect. The evidence on both sides is carefully considered, and throughout is felt a constant appeal for more openmindedness on the part of the workers in this field and the necessity for new evidence to weigh. Perhaps the greatest value of the book is that it may serve as an antidote to dogmatic doctrines of metabolism which are stressed so much in writing of the present day.

Directory of Pediatric Societies

NATIONAL

AMERICAN MEDICAL ASSOCIATION, SCIENTIFIC ASSEMBLY, SECTION ON DISEASES OF CHILDREN

Chairman: Dr. W. A. Mulherin, 753 Broad St., Augusta, Ga.
Secretary: Dr. C. A. Aldrich, 545 Lincoln Ave., Winnetka, Ill.
Place: Portland, Ore. Time: July 8-12, 1929.

AMERICAN PEDIATRIC SOCIETY

President: Dr. Joseph Brennemann, 30 N. Michigan Blvd., Chicago.
Secretary-Treasurer: Dr. Howard Childs Carpenter, 1805 Spruce St., Philadelphia.
Place: Montreal. Time: May or June, 1930.

THE ASSOCIATION OF AMERICAN TEACHERS OF THE DISEASES OF CHILDREN

President: Dr. Paul W. Emerson, 86 Bay State Road, Boston.
Secretary: Dr. Ralph M. Tyson, 1527 Pine St., Philadelphia.
Place: Portland, Ore. Time: July 8-12, 1929.

AMERICAN CHILD HEALTH ASSOCIATION

President: Hon. Herbert Hoover, 370 7th Ave., New York.
Secretary: Dr. Philip Van Ingen, 370 7th Ave., New York.
Place: Minneapolis. Time: Sept. 30-Oct. 4, 1929.

CANADIAN SOCIETY FOR THE STUDY OF DISEASES OF CHILDREN

President: Dr. Thomas Crossan Clark, 51 Herkimer St., Hamilton, Ont.
Secretary-Treasurer: Dr. Frank H. Boone, 164 James St. S., Hamilton, Ont.

SECTIONAL

CENTRAL STATES PEDIATRIC SOCIETY

President: Dr. J. Gurney Taylor, 120 E. Wisconsin St., Milwaukee.
Secretary: Dr. A. H. Parmelee, 310 S. Michigan Ave., Chicago.
Place: Milwaukee. Time: October, 1929.

SECTION ON PEDIATRICS OF SOUTHERN MEDICAL ASSOCIATION

Chairman: Dr. J. H. Eugene Rosamond, 1074 Madison Ave., Memphis, Tenn.
Secretary: Dr. A. J. Waring, De Renne Apts., Savannah, Ga.
Place: Miami, Fla. Time: Nov. 20-22, 1929.

LOCAL

ALABAMA PEDIATRIC SOCIETY

President: Dr. J. MacBell, Mobile.
Secretary-Treasurer: Dr. Hughes Kennedy, Jr., Highland Plaza Apts., Birmingham.

NORTHERN CALIFORNIA PEDIATRIC SOCIETY

President: Dr. W. L. Channell, Medical Bldg., Oakland.
Secretary: Dr. J. E. Parrott, Medico-Dental Bldg., San Francisco.
Place: Various teaching schools. Time: Monthly.

SOUTHWESTERN PEDIATRIC SOCIETY

President: Dr. Ezra S. Fish, Pacific Mutual Bldg., Los Angeles.
Secretary: Dr. Fred L. Glascock, 1136 W. 6th St., Los Angeles.
Place: University Club of Los Angeles. Time: First Wednesday in January, March, May, September and November.

THE ROCKY MOUNTAIN PEDIATRIC SOCIETY

President: Dr. Elsie Seelye Pratt, Republic Bldg., Denver.
Secretary and Treasurer: Dr. Wilford W. Barber, Metropolitan Bldg., Denver.
Place: Children's Hospital, Denver. Time: Third Saturday of each month from September to May, inclusive, 2:30 p. m.

GEORGIA PEDIATRIC SOCIETY

President: Dr. W. N. Adkins, Medical Arts Bldg., Atlanta.
Secretary and Treasurer: Dr. E. N. Gleaton, 212 E. Gaston St., Savannah.

PEDIATRIC SECTION OF FULTON COUNTY MEDICAL SOCIETY, ATLANTA, GA.

Chairman: Dr. Lee Bivings, Exchange Bldg., Atlanta.
Secretary: Dr. William Kiser, Medical Arts Bldg., Atlanta.
Place: Academy of Medicine, 32 Howard St. Time: Second Thursday of each month from October to April, 8 p. m.

NEW ENGLAND PEDIATRIC SOCIETY

President: Dr. Edwin T. Wyman, 483 Beacon St., Boston.
Secretary-Treasurer: Dr. Randolph K. Byers, 66 Commonwealth Ave., Boston.
Place: Boston Medical Library. Time: Second Friday of each month.

CHICAGO PEDIATRIC SOCIETY

President: Dr. Maurice Blatt, 185 N. Wabash Ave., Chicago.
Secretary: Dr. J. K. Calvin, 104 S. Michigan Ave., Chicago.
Place: City Club. Time: Third Tuesday of each month.

LOUISIANA STATE PEDIATRIC SOCIETY

President: Dr. J. A. Crawford, Lake Charles.
Secretary-Treasurer: Dr. C. T. Williams, 7401 Burthe St., New Orleans.

DETROIT PEDIATRIC SOCIETY

President: Dr. M. Boyd Kay, 10 Peterboro St., Detroit.
Secretary: Dr. Charles A. Wilson, 71 E. Ferry St., Detroit.
Place: Children's Hospital of Michigan. Time: No fixed date; approximately once a month.

NORTHWESTERN PEDIATRIC SOCIETY

President: Dr. C. R. Moriarity, La Salle Bldg., Minneapolis.
Secretary: Dr. E. S. Platou, 730 La Salle Bldg., Minneapolis.
Place: University Campus and Rochester, Minn. Time: Winter, Spring, Summer, Fall.

ST. LOUIS PEDIATRIC SOCIETY

President: Dr. Park J. White, Beaumont Bldg., St. Louis.
Secretary-Treasurer: Dr. Ralph L. Cook, 508 N. Grand Blvd., St. Louis.
Place: St. Louis Children's Hospital. Time: At least once a year and contingent thereafter on the arrangement of a suitable program.

NEBRASKA-IOWA PEDIATRIC SOCIETY

President: Dr. Floyd Clarke, City Nat'l Bank Bldg., Omaha.
Secretary: Dr. R. B. Eldredge, Medical Arts Bldg., Omaha.
Place: Add-Sell Restaurant. Time: Second Thursday of each month from October to May, inclusive, 6 p. m.

BROOKLYN PEDIATRIC SOCIETY

President: Dr. Louis M. Ruderman, 961 Eastern Pkwy., Brooklyn.
Secretary: Dr. Joseph F. Paulonis, 1357 Bushwick Ave., Brooklyn.
Place: Kings County Medical Society Bldg. Time: Last Wednesday of each month, except June, July and August.

BRONX PEDIATRIC SOCIETY

President: Dr. L. H. Barenberg, 1749 Grand Concourse, New York.
Secretary: Dr. Joseph Golomb, 496 E. 175th St., New York.
Place: Concourse Plaza, 161st St. and Grand Concourse, New York. Time: Second Wednesday of each month, except June, July, August and September.

CENTRAL NEW YORK PEDIATRIC CLUB

President: Dr. Frank Vander Bogert, 111 Union St., Schenectady.
Secretary: Dr. Frank J. Williams, 58 S. Swan St., Albany.
Place: Various cities in New York. Time: Fourth Thursday of October, January and April.

NEW YORK ACADEMY OF MEDICINE, SECTION OF PEDIATRICS

President: Dr. F. Elmer Johnson, 300 West End Ave., New York.
Secretary: Dr. Hugh Chaplin, 39 E. 75th St., New York.
Place: New York Academy of Medicine, 2 E. 103d St. Time: Second Thursday of each month from October to May, inclusive, 8:30 p. m.

ROCHESTER PEDIATRIC SOCIETY

President: Dr. John Aikman, 184 Alexander St., Rochester, N. Y.
Secretary: Dr. Howard F. Rowley, 278 Alexander St., Rochester, N. Y.
Place: Arranged by program committee. Time: First Friday of each month from October to May.

ACADEMY OF MEDICINE OF CLEVELAND, PEDIATRIC SECTION

Chairman: Dr. C. W. Wyckoff, 8314 Euclid Ave., Cleveland.
Secretary: Dr. C. L. Ruggles, 10616 Euclid Ave., Cleveland.
Place: 2009 Adelbert Road. Time: Four meetings, from September to May.

PHILADELPHIA PEDIATRIC SOCIETY

President: Dr. Ralph M. Tyson, 334 S. 21st St., Philadelphia.
Secretary: Dr. John D. Donnelly, 115 Bryn Mawr Ave., Bala-Cynwyd, Pa.
Place: College of Physicians, 19 S. 22d St. Time: Second Tuesday of each month from October to June, inclusive.

PITTSBURGH PEDIATRIC SOCIETY

President: Dr. Zaccheus R. Scott, Westinghouse Bldg., Pittsburgh.
Secretary: Dr. Theodore C. Elterich, Highland Bldg., Pittsburgh.
Place: Pittsburgh Academy of Medicine. Time: Second Friday, alternate months.

THE SOUTH CAROLINA PEDIATRIC SOCIETY

President: Dr. E. A. Hines, Seneca.
Secretary-Treasurer: Dr. R. M. Pollitzer, 105 E. North St., Greenville.

MEMPHIS PEDIATRIC SOCIETY

President: Dr. A. G. Quinn, 1193 Madison Ave., Memphis, Tenn.
Secretary: Dr. Kinsey M. Buck, 1024 Madison Ave., Memphis, Tenn.
Place: Memphis General Hospital. Time: Second Tuesday of each month.

TEXAS PEDIATRIC SOCIETY

President: Dr. Edwin G. Schwarz, Medical Arts Bldg., Fort Worth.
Secretary-Treasurer: Dr. Ramsey Moore, Medical Arts Bldg., Dallas.

RICHMOND PEDIATRIC SOCIETY

President: Dr. J. B. Stone, 2042 Park Ave., Medical Arts Bldg., Richmond, Va.
Secretary-Treasurer: Dr. Samuel A. Anderson, Jr., 2326 W. Grace St., Richmond, Va.
Place: Westmoreland Club, 601 E. Grace St. Time: First Thursday of each month (other than during the summer).

VIRGINIA PEDIATRIC SOCIETY

President: Dr. Charles E. Conrad, Harrisonburg.
Secretary: Dr. William B. McIlwaine, Petersburg.

NORTH PACIFIC PEDIATRIC SOCIETY

President: Dr. E. D. Carder, 736 Granville St., Vancouver, B. C.
Secretary and Treasurer: Dr. George A. Lamont, 736 Granville St., Vancouver, B. C.

SEATTLE PEDIATRIC SOCIETY

President: Dr. Arthur H. Gray, Lumber Exchange Bldg., Seattle.
Secretary: Dr. Armin Rembe, Stimson Bldg., Seattle.
Place: College Club. Time: Third Friday of each month, 7 p. m.

MILWAUKEE PEDIATRIC SOCIETY

President: Dr. A. L. Kastner, 120 E. Wisconsin St., Milwaukee.
Secretary: Dr. F. R. Janney, 418 E. North Ave., Milwaukee.
Place: Children's Hospital. Time: Second Wednesday of each alternate month, beginning with February.

ACADEMY OF MEDICINE, TORONTO, SECTION OF PEDIATRICS

President: Dr. G. A. Davis, 12 Belsize Drive, Toronto.
Secretary: Dr. Gladys Boyd, 56 DeLisle St., Toronto.
Time: November 17, December 15, February 16 and March 15.

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